

**UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA**

UNITED STATES OF AMERICA,)	Civil Action No. 99-CV-02496 (GK)
Plaintiff,)	
v.)	Next scheduled appearance:
PHILIP MORRIS USA INC.,)	Trial (ongoing)
f/k/a PHILIP MORRIS INC, <u>et al.</u> ,)	
Defendants.)	
)	

WRITTEN DIRECT EXAMINATION OF:

MICHAEL WEITZMAN, M.D.

SUBMITTED PURSUANT TO ORDER # 471

1 **Q. Could you please state your full name for the record?**

2 A. Michael Lane Weitzman.

3 **Q. Where do you currently live?**

4 A. 141 Grovesnor Road, Rochester New York.

5 **Q. Where do you currently work?**

6 A. I work as the Executive Director of the American Academy of Pediatrics Center for Child
7 Health Research.

8 **Q. Do you hold any other positions?**

9 A. I am professor and associate chair of the Department of Pediatrics at the University of
10 Rochester School of Medicine and Dentistry. I am also the director of two federally funded
11 fellowship training programs in academic general pediatrics.

12 **Q. Let's discuss your educational background. From where did you receive your**
13 **undergraduate degree?**

14 A. From Brooklyn College.

15 **Q. What year did you graduate?**

16 A. I graduated in 1968.

17 **Q. Where did you attend medical school?**

18 A. The State University of New York Upstate Medical Center in Syracuse, New York.

19 **Q. What year did you graduate?**

20 A. I graduated in 1972.

21 **Q. Are you board certified in any specialty?**

22 A. Yes, I am board certified in Pediatrics.

23 **Q. What is involved in obtaining your board certification?**

24 A. I obtained my board certification in pediatrics through an accredited residency training

1 program and by sitting for both written and oral boards in pediatrics.

2 **Q. Where did you perform your internship?**

3 A. At the State University of New York Upstate Medical Center in Syracuse, NY.

4 **Q. In what year did you perform your internship?**

5 A. 1972 – 1973.

6 **Q. And where did you perform your residency?**

7 A. Also at the State University of New York Upstate Medical Center campus.

8 **Q. And in what specialty did you perform your residency?**

9 A. Pediatrics.

10 **Q. What year did you complete your residency?**

11 A. 1975.

12 **Q. Did you receive any honors during your residency?**

13 A. I was chosen to serve as the chief resident for the training program.

14 **Q. Besides your hospital activities, what else did you do during your residency?**

15 A. During my residency, I began and ran the first Lead Poisoning Treatment Program in the
16 Syracuse area. As head of the Program, I was responsible for admitting patients and overseeing
17 their treatment for lead poisoning.

18 **Q. Can you provide some specifics regarding this program?**

19 A. The Childhood Lead Poisoning Treatment Program provided the medical care for all
20 children with elevated blood lead levels referred from practicing pediatricians in the Syracuse
21 area. In 1971, the Onodoga County Health Department received a grant from the CDC in order
22 to begin screening children for lead poisoning. Children whose screening tests revealed high
23 levels of lead were referred to the hospital for further diagnostic testing and treatment.

24 **Q. What did you do following the completion of your residency?**

1 A. When I left my residency, in addition to attending the Maxwell School of Public Health
2 Administration, I attended on the ward supervising resident activity concerning hospitalized
3 children and continued to run the Childhood Lead Poisoning Treatment Program.

4 **Q. When did you leave that position?**

5 A. I left that position in 1976 to move to Boston where I was a Research Fellow in the
6 Department of Health Services at the Harvard School of Public Health between 1976 and 1977.
7 During that time, I received training in research methodology.

8 **Q. Did you hold any other positions during this time period?**

9 A. I served as a faculty member and clinician at the Boston Children's Hospital Medical
10 Center, where I had the title of Assistant Visiting Physician. I also achieved the rank of Assistant
11 Professor in the Dept. of Health Services in the Harvard School of Public Health between 1977
12 and 1979.

13 **Q. What is an Assistant Visiting Physician?**

14 A. It is a title given to physicians with privileges to admit patients to Boston Children's
15 Hospital Medical Center.

16 **Q. What were your duties in that position?**

17 A. My responsibilities included taking care of my own panel of patients in the outpatient
18 department of Boston Children's Hospital Medical Center, caring for these patients when they
19 were admitted to the hospital, taking night call for all clinic patients, and supervising the clinical
20 education of residents and fellows at the Boston Children's Hospital Medical Center as well as
21 medical students from the Harvard Medical School.

22 **Q. When did you leave that position?**

23 A. I left that position in 1979.

24 **Q. Any other employment during this time period?**

1 A. I worked one evening per week and one weekend per month caring for adults with severe
2 developmental disabilities at the Fernald State School in Waltham, Massachusetts.

3 **Q. What did you do following this job?**

4 A. In 1979, I moved to the Boston University School of Medicine Department of Pediatrics
5 as an Assistant Professor. I proceeded to stay at the school in a variety of roles until 1990.

6 **Q. And how did you obtain that position?**

7 A. I was recruited by the Chairman of the Dept. of Pediatrics at Boston University and
8 Boston City Hospital.

9 **Q. What were your duties in that position?**

10 A. In the ten years that I was at Boston City Hospital and Boston University, I had a variety
11 of roles. Generally, across all ten years, I continued to see and care for my own panel of patients
12 in an outpatient setting, took night call on a regular basis, and cared for patients when they were
13 hospitalized at Boston City Hospital.

14 **Q. Any other duties?**

15 A. For those 10 years, I also supervised residents and medical students caring for patients.

16 **Q. What was your position when you started at Boston University?**

17 A. I started as an Assistant Professor in 1979.

18 **Q. Were you ever promoted?**

19 A. Yes, I was promoted to Associate Professor of both Pediatrics and Public Health in 1984.
20 I was promoted to the position of Professor of Pediatrics at the Boston University School of
21 Medicine. After moving to the University of Rochester, I carried the title of Adjunct Associate
22 Professor of Public Health.

23 **Q. Did you have any other teaching duties?**

24 A. Yes, I did. For a five year period from 1985 until 1990, I taught a number of courses at

1 the Boston University School of Public Health.

2 **Q. While at Boston University, did you have any duties outside of teaching?**

3 A. In addition to my academic promotions, I was actively involved in clinical care, public
4 health education, and research.

5 **Q. During this period, did you have any jobs outside of Boston University itself?**

6 A. I served as the Director of Maternal and Child Health Services for the City of Boston. In
7 this capacity I oversaw all maternal and child health services run by the Health Department
8 including home visitation programs, Sudden Infant Death Syndrome programs, lead poisoning
9 and injury prevention programs.

10 **Q. Any other outside duties?**

11 A. I also became the Director of General Pediatrics during this period in which capacity I
12 was responsible for the clinical care provided to all outpatients at Boston City Hospital who were
13 children and for the career development of the faculty. I also was involved in a number of large
14 scale research projects funded both by private foundations and federal agencies.

15 **Q. Any other duties that you'd wish to discuss?**

16 A. I also wrote the grant and ran the program that trained academic general pediatric faculty.

17 **Q. When did you leave these jobs?**

18 A. I left these jobs in 1990.

19 **Q. What was your next position?**

20 A. When I moved to Rochester, New York, I assumed a number of positions. I was
21 appointed as a Professor and Associate Chair of the Department of Pediatrics at the University of
22 Rochester School of Medicine and Dentistry, where I also carried the titles of Director of the
23 Division of General Pediatrics, Fellowship Director for Academic General Pediatrics at the
24 University, and Pediatrician-In-Chief at the Rochester General Hospital, a large hospital that has

1 about 40,000 pediatric visits per year.

2 **Q. How did you obtain this position?**

3 A. There was a national search and the search committee reached out to me to see if I was
4 interested. I then interviewed for the position and was, fortunately, offered it.

5 **Q. What were your duties in this position?**

6 A. As Pediatrician-In-Chief at the Rochester General Hospital, I oversaw all aspects of the
7 care of all children who came to that institution to our ambulatory care center, our emergency
8 room, our inpatient unit, and for all newborns born at our hospital.

9 **Q. Was there extensive pediatric care available at Rochester General?**

10 A. All levels of pediatric care, short of intensive care unit therapy, were available at
11 Rochester General Hospital. We had an inpatient unit for children and adolescents, a well baby
12 nursery, a level 2 nursery, an outpatient department, and a pediatric emergency room.

13 **Q. Did you have any other duties in this position?**

14 A. As Pediatrician-In-Chief, I also was responsible for the career development of
15 approximately two dozen members of the department, as well as for all medical student and
16 resident education that went on at this hospital. Because all University of Rochester residents in
17 pediatrics spend a third of their residency at Rochester General Hospital, I was responsible for
18 the clinical care they provided and overseeing the education that they received.

19 **Q. How long did you serve in this position?**

20 A. I served in this capacity for 9 years.

21 **Q. In this nine-year period did you hold any other positions?**

22 A. In addition to being the Pediatrician-In-Chief at Rochester General, I was the Director of
23 the Division of General Pediatrics. In that capacity, I was responsible for the clinical care and
24 career development for the around thirty faculty members located at two separate hospitals and

1 the quality of care that they provided. In addition, I served as the Associate Chairman for
2 Community Affairs for the Department of Pediatrics at the medical school and directed the
3 fellowship program in Academic General Pediatrics.

4 **Q. What were your duties as Associate Chairman for Community Affairs?**

5 A. As Associate Chairman for Community Affairs, I oversee relations and collaborations
6 between the Department of Pediatrics and all community pediatricians. In that capacity, I
7 represent the department in its interface with clinical pediatricians around issues that concern the
8 care of children in community settings. As an Associate Chair, I also am part of the Executive
9 Committee of the Department of Pediatrics, and am heavily involved in decision making at the
10 highest level for the department.

11 **Q. Do you still hold that position?**

12 A. Yes, I still hold that position.

13 **Q. Did you hold any other positions?**

14 A. I was also Director of the fellowship program for General Academic Pediatrics.

15 **Q. What does the term "General Academic Pediatrics" mean?**

16 A. General Academic Pediatrics refers to hospital and medical center based academic
17 pediatricians who provide medical care to the children who come to the hospital for their care.
18 These children are largely minorities and poor children. These doctors are also responsible for
19 the majority of education that medical students and residents receive in outpatient pediatrics.
20 Finally, they also tend to perform the majority of non-bench research concerning children's
21 health.

22 **Q. What is non-bench research?**

23 A. It is clinical research, focusing on epidemiology and health services. For example, a
24 bench researcher might do basic science to invent a new vaccine for meningitis in children.

1 General academic pediatricians doing research in clinical epidemiology could then evaluate how
2 well the vaccine works to prevent disease, and then do health services research to determine why
3 people are not receiving the vaccine and how those barriers can be overcome. General academic
4 pediatricians could also perform the original work describing the clinical features of the
5 particular type of meningitis and the extent of its impact in the population and risk factors for bad
6 outcomes.

7 **Q. So, there is a lot of medical research done to improve children's health that is not**
8 **performed in laboratories?**

9 A. Yes. People tend to think of medical research involving just the laboratory experiments,
10 but even with a new drug, there's a lot of scientific work going on before and after the lab
11 research. In fact, when you are talking about prevention at the population level, the research may
12 not involve bench science at all.

13 **Q. How long did you hold that position?**

14 A. I was Director of the Division of General Pediatrics at the University of Rochester for 9
15 years.

16 **Q. Getting back to your current position, you are now the Executive Director of the**
17 **American Academy of Pediatrics' Center for Child Health Research?**

18 A. Yes.

19 **Q. What is the Center for Child Health Research?**

20 A. The Center for Child Health Research is an independent operating branch of the
21 American Academy of Pediatrics, the professional organization that represents this nation's
22 pediatricians. The Center for Child Health Research is the only national center for child health
23 research in the United States, as well as the only research center that is affiliated with a
24 professional group of physicians.

1 **Q. Why was it established?**

2 A. The Center for Child Health Research was created by the American Academy of
3 Pediatrics because it recognized that the health problems of the nation's children were too great
4 to be dealt with by one professional group alone. Thus, the Academy created the Center with
5 three overarching goals.

6 **Q. What were those goals?**

7 A. The first was to identify and champion, both to funders and the pediatric research
8 community, priority areas for child health research. The second was to stimulate, catalyze,
9 coordinate, and conduct that research. The third priority was to synthesize information and
10 identify new methods by which information that would improve the health of the nation's
11 children would be identified and implemented.

12 **Q. Who is involved in these activities?**

13 A: One group involved is an independent Board of Directors, which includes three members
14 from the American Academy of Pediatrics, an association of pediatricians which has over 60,000
15 members. The remaining nine board members are selected from the leading researchers and
16 scholars concerning child health from across the nation.

17 **Q. Who are some of these researchers and scholars?**

18 A. They include former Surgeon General Julius Richmond, Cathy DeAngelis (Editor of the
19 Journal of the American Medical Association), and many other luminaries from within the fields
20 of pediatrics, law, family practice, and health policy.

21 **Q. Who else is involved with the Center's activities?**

22 A. In addition to the Board of Directors, the Center has approximately 10 people working on
23 Center related activities and on the budget at the University of Rochester. They include a
24 medical student from the University of Rochester who has taken a year out to work on research

1 involved in the Center.

2 **Q. Can you more specifically describe the Center's employees, please?**

3 A. The Center has approximately 10 employees at the University of Rochester,
4 approximately another 10 employees at the American Academy of Pediatrics, one full time
5 faculty member and a secretary at the University of Vermont, and then a series of collaborations
6 with people located around the country.

7 **Q. Any other personnel?**

8 A. There are increasing numbers of medical students who participate in research projects at
9 the Center but they are not employees.

10 **Q. Does the Center work with any outside child health researchers?**

11 A. As a national child health center, the Center collaborates with over 100 other researchers
12 from other institutions around the country. In addition, the Center collaborates with a cadre of
13 social scientists who are located in Chicago who work on developing measures of functional
14 status of children. Finally, we have the Pediatric Research in the Office Setting Network, which
15 consists of over 2000 pediatricians in practice who participate in office-based research doing
16 important work on violence prevention, counseling, recognition of child abuse by pediatricians,
17 ways to increase immunization rates of children, and more recently on obesity prevention,
18 tobacco cessation and in the past, age of onset of puberty in girls.

19 **Q. What are some of the pediatric issues that the Center has researched?**

20 A. The Center in its first five years has published approximately 90 peer-reviewed journal
21 articles and a number of books.

22 **Q. What were the subjects of the articles?**

23 A. The research papers we have published have focused on subjects such as preventive
24 health services for children, the needs of Latino children in the United States, a number of mental

1 health issues of children, obesity, the influences of tobacco and environmental tobacco smoke on
2 children, and the attitudes of the public towards pediatricians becoming more involved in
3 smoking cessation activities for parents.

4 **Q. Any other papers relating to smoking and children?**

5 A. The tobacco influences have included a paper in the *Journal of the American Medical*
6 *Association* on the relationship between parental smoking and dental caries in children as well as
7 a number of other papers concerning environmental health influences on children.

8 **Q. What are some of the books the Center has prepared?**

9 A. In October, the Center will publish a book entitled, About Children, which is aimed at
10 policymakers at all levels in the United States and discusses many of the most important social
11 and environmental influences on child health and well-being. It is being published as a
12 centerpiece of the American Academy of Pediatrics 75th Anniversary celebration. In addition,
13 last month we published, along with Child Trends, a major social science research institution in
14 the Washington DC area, a book entitled, Early Childhood Development in a Social Context.
15 This book reviewed many of the most important malleable influences on child development and
16 school readiness. Finally, earlier this year we also published a Supplement to *Pediatrics* on the
17 unique vulnerabilities and resiliencies of children to environmental influences.

18 **Q. When will the Supplement be published?**

19 A. The Supplement was published in April, 2004. It had over 30 papers with over 50
20 authors, who were nationally or internationally known authorities in their field. As the person
21 who received the grant from the EPA, I chose my co-editor and the majority of topics and
22 individuals to write on those topics. I also oversaw the administration of correspondence with
23 them, the distribution of manuscripts for outside review, and the final coordination and approval
24 for the articles.

1 **Q. What else does the Center do?**

2 A. The Center also informs the pediatric community about new information that is being
3 generated and works to link the pediatric community to other professional groups doing research
4 concerning the well-being of children.

5 **Q. How is it funded?**

6 A. The Center is funded with modest infrastructure support by the American Academy of
7 Pediatrics, the University of Rochester, and through grants obtained from the federal government
8 and from private foundations.

9 **Q. From what federal agencies does the Center receive funding?**

10 A. The center has received funding from the following federal agencies: The Maternal and
11 Child Health Bureau, the Centers for Disease Control and Prevention, the Agency for Health
12 Research and Quality, the National Institutes of Health, and the Environmental Protection
13 Agency.

14 **Q. From what private foundations does the Center receive funding?**

15 A. The Center has received funding from the Robert Wood Johnson Foundation, the
16 American Legacy Foundation, and the Commonwealth Foundation.

17 **Q. What are your duties with regard to the Center?**

18 A. My duties are those of an Executive Director, who oversees the work of all the
19 individuals in the Center. As such, I am responsible for the hiring of employees as well as the
20 identification and implementation of much of the large national dataset research. In addition, I
21 am responsible for the identification of priority areas for research, as well as the proper child
22 health researchers to work on that research.

23 **Q. Any other duties?**

24 A. I also oversee the convening of the multiple groups that we bring together concerning

1 mental health issues of children, income and equality of child well being, Latino children's
2 health, tobacco as a pediatric issue, the interface of information technology and pediatrics, and a
3 number of other issues. I have also been responsible for identifying most of the authors for our
4 book entitled, About Children.

5 **Q. Are you involved with any public speaking on Center issues?**

6 A. Yes. I have given numerous speeches on tobacco-related topics both in the United States
7 and abroad. Most recently, I discussed the effects of tobacco on children's health at the annual
8 meeting of the Japanese Society of Ambulatory and General Pediatrics in Oita City, Japan. I
9 have also presented the Center's findings regarding tobacco at the National Conference on
10 Tobacco and Health in Washington, D.C. in 2003. There are numerous other talks that I have
11 given regarding tobacco and its effects on children's health, including speeches for the Centers
12 for Disease Control, the Maternal and Child Health 2010 Conference, the National Initiative for
13 Children's Healthcare Quality, and the Pediatric Academic Societies.

14 **Q. How did you end up in your current position?**

15 A. There was a national search by the American Academy of Pediatrics for an Executive
16 Director. Because of my visibility in the academic and research world, as well as the American
17 Academy of Pediatrics, I was asked to interview for this position and I was chosen by the Search
18 Committee.

19 **Q. How were you visible in the academic and research world?**

20 A. My visibility was due to my longstanding experience as a general pediatrician who did
21 research and because of my activities with the American Academy of Pediatrics.

22 **Q. Please describe those activities.**

23 A. At the Academy, I had been a member of and directed the Committee on Community
24 Child Health Services, which is the committee that establishes policy statements for socially

disadvantaged children in the United States, including homeless children, illegal immigrant children, immigrant children in general, and migrant farmer laborer children.

Q. You mentioned your teaching experience. Are you currently teaching any classes at the medical school?

A. I co-teach a course involving an overview of health services research that extends through most of the academic year for our fellows in Academic General Pediatrics, Adolescent Medicine, as well as PhD. students from the School of Nursing and for child psychology and psychiatry fellows. I also teach in several classes in the Department of Community and Preventive Medicine, and present grand rounds regularly. Finally, I attend morning report with our residents one to three mornings each week, supervise and teach residents in our continuity clinic at the University of Rochester as they provide care to patients ½ day per week, and attend on the inpatient ward once per year for two weeks.

Q. Any other teaching responsibilities?

A. I oversee our two fellowship training programs in academic general pediatrics, with 5-7 fellows per year. They are located with me and I oversee all aspects of their training as fellows.

Q. Do you yourself conduct any research?

A: Yes. I conduct research on a wide variety of child health issues. These issues have included tobacco influences on children, the attitudes of pediatricians towards tobacco counseling, obesity in children, child mental health, and health preventive services for children.

Q. In your years as a health researcher and professional, have you received any awards?

A. I have won a number of awards through the years. I have won the Research Award from the Ambulatory Pediatric Association, its most prestigious award for lifetime achievement in research.

1 **Q. What is the Ambulatory Pediatric Association?**

2 A. The Ambulatory Pediatric Association is the professional organization of the 2,000
3 academic pediatricians around the nation.

4 **Q. For what research did you receive this award?**

5 A. It was for my lifetime body of research on child health issues.

6 **Q. Any other awards from this Association?**

7 A. I also have won the teaching award from the Ambulatory Association in recognition of
8 more than ten years of running the two federally funded Academy General Pediatrics Fellowship
9 programs at the University of Rochester.

10 **Q: Is it unusual to win both awards?**

11 A. Yes. I am the only member out of the 2,000 members of the Ambulatory Pediatric
12 Association to have won both the research award and its teaching award.

13 **Q. Have you won any other teaching awards?**

14 A. Yes. I won the Boston University Faculty Teaching Award.

15 **Q. Why did you win this award?**

16 A. The Boston University Faculty Teaching Award was a consequence of being voted by the
17 pediatric trainees at the Boston University School of Medicine as the best faculty teacher.

18 **Q. Any other honors or awards?**

19 A. This past year, I was elected to the Best Doctors in America. In addition, I have been
20 appointed to prestigious national committees that are a consequence of meticulous reviews
21 involving experts in various fields. Among these are my previous service on the Centers for
22 Disease Control and Prevention Committee on Children With Disabilities, my appointment and
23 service on the Advisory Committee on Childhood Lead Poisoning Prevention Center for five
24 years at the Centers for Disease Control and Prevention, my selection as overseer for the CDC's

1 workgroup on the Effects of Low Level Lead on Children.

2 **Q. Any others?**

3 A. I served on the Advisory group to the Children's Health Protection Branch of the
4 Environmental Protection Agency, and as an ad hoc reviewer for the National Institute of Child
5 Health and Development. Finally, I currently serve on the Institute of Medicine's committee on
6 Ethical Issues Involved in Housing Related Research of Children and have been and continue to
7 serve on the National Advisory Committee of the Robert Wood Johnson Foundation Generalist
8 Faculty Scholars Program.

9 **Q. What is the National Advisory Committee's purpose?**

10 A. The National Advisory Committee of the Robert Wood Johnson Generalist Faculty
11 Scholars Program is the committee that runs this national career development program for young
12 faculty members in generalist fields in medical schools around the United States in family
13 practice, internal medicine and pediatrics. The Committee's responsibility includes the review of
14 all applications for this program, the interviewing of applicants and the choosing of them, and
15 mentoring them.

16 **Q. What exactly did the Ethics of Research on Children's Housing involve?**

17 A. The Institute of Medicine Committee of Ethics of Research on Children's Housing is
18 putting together, as the Institute of Medicine does for a large number of issues, a summary
19 document about what are the ethical obligations of researchers who are doing research on various
20 aspects of children's homes. Any time one visits one's home as part of research; there are
21 different obligations that kick into play that would not come up in clinically situated biomedical
22 research.

23 **Q. How much time did this activity involve?**

24 A. I probably spend on average half a day a week, almost exclusively done in the evenings

1 and weekends, on this for the past several months. This pattern of activity will continue at least
2 for the next several months.

3 **Q. How long did you serve on this Committee?**

4 A. I have been on this committee for approximately one year and I believe that it goes for
5 another 12 to 18 months.

6 **Q. Any other government-related activities?**

7 A. I am an Ad Hoc reviewer for National Institute of Child Health and Development.

8 **Q. What are you reviewing for this institution?**

9 A. I review grant applications for a variety of types of grants that are submitted by academic
10 individuals from Universities around the country for federal funding for research that deals with
11 children's issues.

12 **Q. What type of grant applications?**

13 A. During the grant review cycle that I most recently participated in, the grants were from
14 researchers investigating issues of better understanding young influences, neurocognition, and
15 school achievement of children.

16 **Q. How much time does this activity take?**

17 A. This activity took approximately one week last year.

18 **Q. Have you ever published any of your research results?**

19 A. Yes. I have published 114 peer reviewed articles and 131 abstracts.

20 **Q. In what journals did these articles appear?**

21 A. They appeared in publications such as *The Journal of American Medical Association*,
22 *Pediatrics*, *The Journal of Pediatrics*, *Archives of Pediatrics and Adolescent Medicine*, and *The*
23 *American Journal of Public Health*, *Neurotoxicology and Teratology*.

24 **Q. Are you being compensated for your work as an expert in this case?**

1 A. No, I am not being compensated personally. The compensation rate of \$300 per hour for
2 my time on this case is being given to the Center so that it can continue its work.

3 **Q. Have you ever previously worked with the federal government on pediatric health**
4 **issues?**

5 A. Yes, I have served in a consultative purpose to the Centers for Disease Control and
6 Prevention and I have served on the CDC's Childhood Lead Poisoning Expert Advisory
7 Committee. I currently lead the CDC's Workgroup on the Effects of Blood Lead Levels Less
8 Than 10 (micrograms per liter) on Children. I served on the CDC's Childhood Disabilities
9 Advisory Committee as well as the Advisory Board to the Environmental Protection Agency's
10 Office of Child Health Protection, and have conducted and published the results of what is
11 known about the interface of information technology and pediatric practice for the Agency for
12 Health Research and Quality. Most recently, I have co-edited and published a supplement to
13 *Pediatrics* on behalf of the Environmental Protection Agency on the state of knowledge about
14 how children's biologic vulnerability to a variety of environmental exposures differs from what
15 we currently know about these exposures effects on adults. As discussed earlier in this
16 testimony, that supplement contains an article summarizing what is known about the effects of
17 prenatal and environmental tobacco smoke on children.

18 **Q. What does the Supplement state on this topic?**

19 A. This article reviews the medical literature regarding both prenatal and postnatal
20 environmental tobacco smoke exposure and its effects on the health of children. It noted that a
21 large body of literature links both prenatal maternal smoking and children's ETS exposure to
22 decreased lung growth, increased rates of respiratory tract infections, otitis media and childhood
23 asthma. There is a dose-response effect, with increased tobacco exposure leading to increased
24 incidence of these problems. Finally, the literature demonstrates that Sudden Infant Death

Syndrome, behavioral problems, neurocognitive deficits, and increased rates of adolescent smoking have all been associated with prenatal and postnatal exposure to smoke.

Q. What did your work for the CDC entail?

A. The work with CDC entailed going to Advisory Committee meetings several times a year usually in Atlanta or Washington, DC, doing presentations and deliberations at those meetings, and working on workgroups that provided recommendations to the public health community and the pediatric community on how to prevent and manage childhood lead poisoning. The work for the Less Than 10 Workgroup entailed identifying and convening some of the leading researchers in the area of children's lead poisoning, air quality measurement, epidemiology, iron deficiency anemia, toxicology and clinical pathology together to review the state of knowledge about low level lead poisoning. Information was provided to the CDC, which will publish it in the *Morbidity and Mortality Weekly Review*.

Q. Have you performed any work for any state or local government agencies?

A. Yes. I have served on the New York State Lead Advisory Committee, and I have convened and published the proceedings of a meeting on Environmental Health on Children in New York State. I have also served on the Massachusetts Maternal and Child Health Advisory Committee for the State Health Department. Finally, I served for five years (1985 to 1989) as the Director of Maternal and Child Health for the City of Boston.

Q. Turning to the opinions you hold in this case, is the issue of tobacco smoke exposure of fetuses and children an important one in the public health community?

A. Yes, it is very important.

Q. How common is this exposure among fetuses and children?

A. Currently, about 11.4 % of all pregnant women smoke during pregnancy.

Q. Why do you believe that this is an important health issue?

1 A. Most women relapse and begin to smoke again after the delivery of a baby. As a result, a
2 more accurate figure is somewhere around 25-30% of children in America whose parents report
3 that they smoke at home. Furthermore, when you look at nationally representative data
4 measuring cotinine levels, cotinine being the major metabolite of nicotine that is degradation
5 product, it is then clear that almost 90% of our children are exposed to secondhand smoke. If we
6 don't continue to pay attention to this and educate the public, they may be overridden by other
7 messages that induce them to smoke during pregnancy and we could lose the progress that we've
8 already obtained.

9 **Q. Why would they be higher than reported?**

10 A. This is because such rates are based on parent report, not serologic evidence.

11 **Q. Is the exposure confined to the prenatal period only?**

12 A. This exposure does not just occur during the prenatal period but occurs throughout life.
13 In fact, despite the fact that 25-30% of American children live in houses with a smoker, you can
14 measure the metabolite of nicotine, cotinine, in almost 90% of America's children using standard
15 laboratory procedures.

16 **Q. Has this tobacco smoke exposure been linked to any child health problems?**

17 A. Secondhand smoke has been linked to many child health problems. It is the leading cause
18 of low birth weight in the United States, accounting for 70% of all low birth weight cases there.

19 **Q. What is the significance of this figure?**

20 A. This has enormous educational and school achievement and economic consequences to it.
21 First, low birth weight babies have more neurocognitive problems. Second, many of them are
22 quite sick and experience a disproportionate use of healthcare services. Third, research has
23 shown that these children go on to do poorly in school. Fourth, it has been well recognized for
24 some time that smoking exposure in the first year of life results in higher rates of pneumonia and

hospitalization at quite an emotional and financial cost. Fifth, this smoking is the leading preventable cause of reoccurring ear infections among children.

Q. Do ear infections form a serious concern for children?

A. Yes, they do. Ear infections are the leading reason why children in the United States receive antibiotics. This creates an enormous economic and public health problem which drives the cost of antibiotics up and also leads to increased rates of bacteria resistant to more common, more familiar, less expensive and less dangerous alternatives. Tobacco smoke exposure is the leading cause of recurrent otitis media and so indirectly endangers the health of the entire world's public. This is due to the emergence of drug resistant bacteria. As a result, it is not science fiction to say that it is within the realm of possibility that there will be emergence of resistant bacteria at some point in the foreseeable future to all antibiotic alternatives that we have available to us.

Q. Are there any other known effects?

A. Other studies have linked it to increased rates of dental caries, diminished lung size, increased rate of risk for the dreaded Metabolic Syndrome among overweight children, which portends type II diabetes and premature cardiac death, and to a number of neurocognitive problems that we will discuss in this testimony.

Q. Has there been scientific literature prepared on this issue?

A. The scientific literature on the relationship between children's neurocognitive development and exposure to prenatal tobacco smoking or environmental smoking or secondhand smoke after birth is quite consistent in showing an association between these exposures and neurotoxic effects on the child.

Q. What does the scientific literature say?

A. That there is a strong and consistent association between prenatal tobacco smoke

1 exposure, secondhand smoke exposure after birth, and behavior problems, mental health
2 problems, and decreased intellectual potential.

3 **Q. Are you familiar with the term “neurotoxic?”**

4 A. Yes, I am.

5 **Q. What does the term neurotoxic mean?**

6 A. Neurotoxic simply means that something is toxic to the nervous system.

7 **Q. Can you explain what the neurotoxic effects maternal smoking causes for children**
8 **are?**

9 A. Yes. The literature points out a concrete number of ways in which maternal smoking is
10 associated with evidence of neurotoxicity of the child. Research has consistently found an
11 alteration both in structure and functioning. The alteration in structure finding was noted in
12 animal studies, and the alteration in function comes from both animal studies and human
13 observational epidemiologic studies.

14 **Q. What structural alterations were discovered?**

15 A. Structurally, nicotine has been found to prematurely shift developing neurons in the brain
16 from proliferation, where immature neurons increase in number, to differentiation, when these
17 neurons take on their specific differential functions. Thus, there are fewer neurons that exist, but
18 the neurons that do exist have increased functioning of specific receptors called nicotinic
19 acetylcholine receptors. This upregulation has been demonstrated to elicit damage in rodent and
20 primate developing brains. In addition, animal studies have demonstrated that chronic nicotine
21 exposure prenatally can disrupt the normal development of the auditory cortex, which is the part
22 of the brain involved in hearing, which is essential to cognitive processing and function.
23 Furthermore, nicotine suppresses the synthesis of DNA in the newborn rat brain, especially in the
24 cerebellum, the part of the brain that controls coordination.

1 **Q. What alterations in functioning were discovered?**

2 A. The studies found irritability, increased hyperactivity, negative responses to the
3 environment in the first several months of life, crying and fussiness, conduct disorders as early as
4 two to three years of age, persistent as well as an increasing amount of conduct disorders and
5 mental health problems as the subjects got older.

6 **Q. Any other findings?**

7 A. The studies also consistently demonstrated findings that are consistent with attention
8 deficit hyperactivity disorder, a condition that affects many American children.

9 **Q. Please describe these findings with a little more detail.**

10 A. In the first such study of its kind to come out of the Human Genome Project, published in
11 the *Journal of Pediatrics* in July, 2003, there has been found to be an increased susceptibility to
12 mother's smoking during pregnancy to rate of developing attention deficit hyperactivity disorder
13 later in childhood amongst children whose mothers had a particular genetic pattern.

14 **Q. Is this finding important?**

15 A. This is a remarkable finding. The very first product of the Human Genome Project to
16 demonstrate long-term behavioral consequences of gene- environmental exposures of children
17 and it is tobacco that is associated with ADHD, which provided a biologic mechanism, if you
18 will, of the strongest sort between the blueprint of life and smoking during pregnancy in putting
19 children at risk. Only certain women that smoke will have children with increased risk. That
20 explains a big piece of the puzzle as to why studies show increased rates of attention deficit
21 activity disorder in children whose mothers smoke but not all such children are affected.

22 **Q. Is this exposure associated with other child health risk factors?**

23 A. Yes, it is associated with other child health risk factors.

24 **Q. What are some of these risk factors?**

1 A. Children whose mothers smoke are also more likely to be exposed to poverty, as well as
2 to less educated and more depressed/anxious mothers.

3 **Q. How do these factors work with tobacco smoke exposure to impact children's**
4 **behavioral and cognitive outcomes?**

5 A. There are many factors in children's life that influence their behavioral and cognitive
6 outcomes. There is child development literature that shows that past a certain number of insults
7 or diminution in capacity and behavior, children have remarkably high rates of probability of
8 falling off the curve and failing in life. Unfortunately, many of these influences are
9 multiplicative in nature.

10 **Q. How are these influences multiplicative in nature?**

11 A. Take for example, tobacco smoke. In a study that we did about kindergarten and first
12 grade retention, we showed if you had a low birth weight, a mother that smoked, behavior
13 problems, and recurrent ear infections, all of which are associated with a mother's smoking, you
14 were almost 10 times more likely to have to repeat kindergarten or first grade.

15 **Q. What are some of the other risk factors for neurocognitive problems?**

16 A. Other risk factors for neurocognitive problems include low birth weight, poorly educated
17 parents, living in a single household, poverty, bad schools, and mental health problems. Each of
18 these factors comes into play with children.

19 **Q. Are most neurocognitive problems caused by only one risk factor?**

20 A. No, they are not. Our tendency to think of one cause resulting in one consequence is
21 oversimplified and it is increasingly recognized that most diseases are multifactorial in nature. In
22 fact, even infectious diseases in many cases, are multifactorial. Not everybody exposed to the
23 agent that causes the disease will get the disease or if they get the disease, there is a wide range of
24 responses.

1 **Q. Can you please provide an example of this?**

2 A. Many of us carry streptococcal bacteria in our heart at all times and don't get a sore throat
3 or rheumatic fever. However, because these risk factors cluster together, they heighten the risk
4 for those kids exposed to tobacco smoke and make it very difficult to separate the effects of each
5 individual risk factor, although by using statistical modeling procedures, one can account for the
6 influence for many of the known things that cluster together.

7 **Q. How do the risk factors heighten the risk for kids exposed to tobacco smoke?**

8 A. Because these risk factors cluster together, they heighten the risk for those kids exposed
9 to tobacco smoke and make it very difficult to separate the effects of each individual risk factor.
10 They also increase the damage done by each of the individual risks.

11 **Q. Have studies been performed to discover why tobacco smoke exposure causes these**
12 **neurocognitive deficits?**

13 A. Yes. Human observational studies and experimental animal studies were performed to
14 build an opus to prove, if you will, that exposure to tobacco prenatally and to secondhand smoke
15 post-natally are associated with and cause neurocognitive deficits.

16 **Q. How do these studies work to provide information on these conditions?**

17 A. Human observational studies and experimental studies build a body of evidence about the
18 association from which the scientific and public health community then draws conclusions about
19 cause.

20 **Q. What specific role do human epidemiologic studies play?**

21 A. Human epidemiologic studies build evidence about the association between the exposures
22 and behavior and cognition in children and adolescents. That literature allows us to weigh in on
23 whether we believe that there is a causal relationship; that is, that it is not just that it occurs more
24 commonly amongst kids with these problems but that we are able to build sufficient evidence

1 that we convince others and ourselves that the evidence is strong enough to believe that the
2 exposure is in fact, causing the problems that we are finding.

3 **Q. What do the human epidemiological studies show?**

4 A. The epidemiologic literature is very consistent demonstrating that children with prenatal
5 and postnatal exposures have increased rates both of mental health problems and neurocognitive
6 problems. As we have already discussed, there are a number of things that tend to co-vary with,
7 compound, and confound the effects of tobacco smoke exposure. Epidemiologic studies become
8 then limited in those areas to identify to everybody's satisfaction that the single, isolated
9 influence is in fact, exposure to tobacco smoke.

10 **Q. Can animal studies help to remedy this confounding?**

11 A. With animal studies, you do not have any of the social confounding of the likelihood
12 being that the subjects who are exposed to tobacco products come from poorer homes with more
13 anxious or depressed parents. In these studies involving mice and monkeys, it is the tobacco
14 smoke that is associated with increased rates of negative outcomes.

15 **Q. Are there difficulties related to experimental animal studies?**

16 A. The problem in using experimental animals is that the human species is extremely
17 complicated, neurocognitively speaking, and so there are certain things that you can feel
18 uncomfortable about by extrapolating from animal studies to humans. There is a difference
19 between a mouse brain and an animal brain such as a monkey or human brain and our ability to
20 measure neurocognitive performance, so one can raise questions about applying these findings
21 definitively to humans. However, if the studies are consistent with epidemiologic findings, then
22 they provide powerful supporting evidence.

23 **Q. Are animal studies better suited for this research?**

24 A. No. The animal models simply provide an additional way to convince individuals of

1 conscience and considerable intelligence in the scientific and medical communities that there is a
2 causal relationship.

3 **Q. Should we just focus on performing animal studies?**

4 A. No. Science is based on research – you search and you search and you search, and if
5 multiple settings, using different methods and populations, come up with similar findings, then
6 you believe the findings are definitive.

7 **Q. What mechanistic questions does maternal smoking evoke in the area of**
8 **neurocognitive functioning?**

9 A. The questions include the actions of nicotine on the fetal brain and the maternal-fetal unit
10 as well as the influence of other toxic smoking agents such as carbon monoxide.

11 **Q. Have animal studies provided sufficient data to implicate any of the agents**
12 **associated with maternal smoking?**

13 A. Yes, animal studies, again, have provided sufficient data to implicate at least nicotine as
14 being causally associated with these findings that we see in epidemiologic studies.

15 **Q. How so?**

16 A. It is remarkable how consistent these animal studies are and how consistent they are with
17 findings in humans. I'm talking about attention, short term memory, hyperactivity, irritability. It
18 also allows us to some extent to see the effects on actual brain anatomy because we cannot
19 dissect the brains of children exposed to smoking in utero or in their homes.

20 **Q. Has there been a focus on any agent?**

21 A. Yes, there has been a focus on nicotine. So, nicotine is the best studied of the numerous
22 chemicals that one is exposed to by active smoking and by passive smoke.

23 **Q. Why this focus on nicotine?**

24 A. The literature has focused on nicotine because it is a well described behavioral teratogen,

1 there is experience utilizing it, and because it is the best understood of all the chemicals in
2 tobacco. In addition, it is the only one that is believed to be associated with the addictive
3 properties of individuals who are smokers and want to smoke but cannot bring themselves to
4 smoke.

5 **Q. What is a behavioral teratogen?**

6 A. A behavioral teratogen is something that a developing organism is exposed to that has
7 long term consequences in behavioral performance with or without evidence of physical
8 pathology.

9 **Q. Are these consequences obvious to an observer?**

10 A. Not always. Such types of behavioral alterations are not always observable to individual
11 observers for a number of discreet reasons. One reason is that they don't occur in all children
12 and so you can't say that there is a one on one effect and tell people that everyone who has a
13 child who was exposed to tobacco smoke is going to have these problems. The other is that they
14 are very subtle and many require application of specific standardized tests which are expensive to
15 develop, and for many of the problems that we uncover, we don't really have therapeutic
16 implications or applications at this point. A third reason is that on a population basis, subtle
17 problems which may or may not influence a particular child may have profound effects on a
18 population basis.

19 **Q. Can you please provide an example of this?**

20 A. That's been our overwhelming concern with lead poisoning for the past twenty years.
21 That is to say, if you are a doctor seeing children with blood lead levels from 10 to 30, which we
22 know diminishes their function and has effects similar to those that nicotine causes, it might
23 seem modest to estimate a 5 or 6% loss for the individual child but it has huge effects when you
24 take a look at the 80 million children in America.

1 **Q. What adverse neurocognitive effects are caused by this nicotine?**

2 A. While we don't know the exact mechanism by which nicotine exerts its effect, animal
3 studies have shown that it accelerates the transition from the stage of brain development that
4 primarily involves proliferation or increase in the number of brain cells, to the stage of
5 differentiation.

6 **Q. Can you please explain this transformation?**

7 A. The brain, like most organs, grows by dividing as a partially differentiated organ and then
8 different parts of it take on specialized activities, or sizes, or shapes, or appearance. These parts
9 have different functions and we know that nicotine shifts brain development from numbers to
10 early differentiation and this involves both the cholinergic nervous system and the adrenergic
11 nervous system.

12 **Q. Is this a complicated process?**

13 A. If this seems complicated, it is because the nervous system is categorized in a number of
14 different ways often by the type of chemical that exists between the end of one cell and the
15 beginning of another in that the release from the first cell leads to stimulation of the second. So
16 in some it is adrenergic or sympathetic and in some it is cholinergic or parasympathetic and in
17 some is dopamine which is the transmitter.

18 **Q. What is dopamine?**

19 A. Dopamine is one of the major neurotransmitters in the nervous system. It acts primarily
20 in two areas of the brain, the basal ganglia and the limbic system. In the basal ganglia, it assists
21 in controlling voluntary movement.

22 **Q. What are the basil ganglia?**

23 A. The basil ganglia are the sections of the brain that function to help the individual with
24 controlling the speed and size of movements. They are also involved in the preparation of the

1 brain and body for movement. In fact, dysfunction of the basal ganglia leads to both voluntary
2 and involuntary movement disorders.

3 **Q. You also mentioned an effect on the limbic system?**

4 A. Yes. In the limbic system, it helps to control emotional responses and memory. In the
5 periphery, it causes vasodilatation at low doses, but can cause vasoconstriction when
6 administered at high doses. Dopamine also stimulates the heart, causing increased cardiac
7 output.

8 **Q. What is the limbic system?**

9 A. The limbic system is the area in the brain that plays a role in mediating the experience of
10 emotions, visceral responses, and the storage of memories. The limbic system has connections
11 with most areas of the brain.

12 **Q. How is dopamine affected by nicotine?**

13 A. Nicotine stimulates dopamine's release in the mesolimbic pathway, which leads to
14 increased locomotor activity. In rats, it has been shown to be a positive reinforcer of nicotine
15 self-administration—when rats were given nicotine, dopamine was released and the rates of
16 further self-administration of nicotine increased.

17 **Q. Are there other ways that dopamine is affected by nicotine?**

18 A. Yes. The dopamine system is influenced in a number of partially understood and
19 complicated ways by nicotine. Nicotine interacts with the dopamine and serotonin systems with
20 the following results: An increase in locomotor activity likely due to nicotine's effects on the
21 hippocampus; an increase in anxiety and impulsivity; an increase in adrenergic binding; attention
22 and memory deficits; a suppression of DNA synthesis; an alteration of levels of N-methyl-D-
23 aspartate receptors (NMDAR) in auditory cortex, which could be the cause for auditory-cognitive
24 processing defects found in children exposed to prenatal nicotine; a decrease in dopamine

activity in ventral tegmental area, nucleus accumbens, striatum; and a decrease in serotonin uptake.

Q. Earlier, you mentioned carbon monoxide as one of the smoke elements that plays a role with neurocognitive impairments?

A. Yes, carbon monoxide is one of the smoking elements that play a role there.

Q. How does it play a role?

A. It is believed to be involved in one of the mechanisms by which smoking during pregnancy results in lower birth weight and diminished head circumference. It inhibits the release of oxygen into fetal tissues.

Q. How exactly does carbon monoxide cause these adverse effects?

A. At the most elementary level, carbon monoxide reduces the availability of oxygen to a developing baby when that baby is in utero with a mother that is smoking. Smoking increases carbon monoxide levels in the blood of the smoker and it crosses the placenta and it also binds with the hemoglobin of the baby. Carbon monoxide binds with hemoglobin more avidly than does oxygen.

Q. What is hemoglobin?

A. Hemoglobin is the enzyme that requires multiple steps for its production that sits inside of red blood cells, and carries oxygen to the tissues.

Q. What happens when the carbon monoxide binds with the hemoglobin?

A. When carbon monoxide binds with the hemoglobin in the mother, less oxygen is available for the baby. Carbon monoxide also transverses the placenta and binds to the baby's hemoglobin even more avidly that it does to the mother's hemoglobin, making the hemoglobin less available to bind oxygen and take that oxygen to the baby's tissues. Carbon monoxide contributes to hypoxia, a decreased oxygen availability for the baby, which in turn also turns on

the developing hematopoietic system of the baby to make more hemoglobin.

Q. What causes this increase in hemoglobin production?

A. The body responds with a whole host of environmental responses or enzyme responses. When you block something that's a chain reaction, the body will increase production of things before that chain reaction in an attempt to compensate.

Q. How was this determined to have occurred in babies?

A. Newborns whose mothers smoked during pregnancy have been found to possess higher hematocrits, a measure of having made more hemoglobin.

Q. What neurobehavioral deficits are associated with this lack of oxygen (hypoxia)?

A. The associated deficits include inattention, repetition types of activities (memorization, counting and sorting objects), hyperactivity, as well as increased distractibility and irritability, and higher rates of occurrence for attention deficit hyperactivity disorder, and oppositional defiance conduct types of disorders.

Q. What percentage of United States children are exposed to secondhand smoke?

A. 11.4 % of children are born to women who report smoking during pregnancy, 25-30% of children live in households with smokers.

Q. Upon what evidence was this estimate based?

A. This evidence is based both upon self-reports of parents in national surveys, reports of women to obstetricians that go onto children's birth certificates, and from estimates drawn from the nationally representative National Health and Examination Survey, which the Centers for Disease Control conducts.

Q. Is it possible that the exposure rate for United States children might be higher?

A. It is possible that children's exposures are higher than the average estimates that we obtain by reports of adults because adults largely know that it is dangerous for parents and others

1 to smoke around children and so in much of our human epidemiologic data there is probably
2 underreporting of smoking. Those that feel the worst about it probably hide it in those particular
3 studies, which only heighten the strength of those studies. The type of error it introduces is that it
4 makes the findings of the published studies far more conservative. That's why the animal studies
5 are so striking in that they so consistently demonstrate in animals' findings that we've found in
6 epidemiologic studies.

7 **Q. What is the result of this misclassification and/or underestimation?**

8 A. The result of this misclassification is an underestimation of the effects or the association
9 or the size of the association of exposure with untoward or undesired neurocognitive outcomes.

10 **Q. If you know, are infants who are exposed to maternal smoking at risk for any other**
11 **toxic exposures?**

12 A. I think that they are exposed at higher rates to higher amounts of lead and I am sure that
13 they are exposed at higher rates to alcohol prenatally, and they are exposed to the toxic effects of
14 maternal depression, anxiety, and a poorly educated mother.

15 **Q. What do these multiple exposures mean for children?**

16 A. These multiple exposures result in two things. For the research or for the legal
17 communities it introduces the issue of potential confounding. That is teasing apart the individual
18 effect of the tobacco from those things that go along with it. For the child, the public health
19 community, the educational community and the health care community, it is one of
20 compounding, as opposed to confounding. That is, each of these have separate negative effects
21 on the child's health and development and as I've noted before, they often have a multiplicative
22 effect and so they cumulatively lead to remarkable differences in disability rates and ability rates,
23 and all sorts of things necessary for health and success in adult life.

24 **Q. How do you know this?**

1 A. I know this as a consequence of researching this information, of writing and editing
2 information related to this, by reviewing this information for the purposes of this case, by
3 teaching it around the United States.

4 **Q. Dr. Weitzman, can maternal smoking have an adverse effect on the infant's birth**
5 **weight?**

6 A. Maternal smoking can have an adverse effect on infant birth weight. In fact, it is the most
7 common cause of low birth weight and it has been estimated to account for about 70% of all low
8 birth weight cases in the United States.

9 **Q. What are some of the other consequences?**

10 A. Maternal smoking has enormous health care, educational, and quality of life
11 consequences for vast numbers of individuals with its contribution to children with medical
12 complications requiring intensive care in the nursery, to increased hospitalization rates, to poor
13 school performance, as well as antisocial types of behavior.

14 **Q. What is the actual impact?**

15 A. There is a 5% reduction in weight per pack of cigarettes smoked per day with an average
16 decrease in weight of 150-300 grams.

17 **Q. How much is that in pounds and ounces?**

18 A. One pound equals 16 ounces, therefore it is a 0.33-0.66 pound reduction or a 5.3-10.6
19 ounce reduction.

20 **Q. So, two packs per day means a 10% decrease in weight?**

21 A. Yes, it does.

22 **Q. From where did this finding result?**

23 A. In 1990, Kramer and colleagues discovered that the effect of prenatal maternal smoking
24 was a 5% reduction in weight per pack of cigarettes smoked per day. Furthermore, Meyer and

1 Comstock reported that the effect of maternal cigarette smoking on infant birth weight caused an
2 average decrease in infant weight of 150-300 grams.

3 **Q. When was this adverse effect first determined?**

4 A. Low birth weight was identified as an adverse effect from prenatal smoking by Simpson
5 in 1957.

6 **Q. Did subsequent studies confirm this association?**

7 A. Literally hundreds and hundreds of subsequent studies have confirmed this association. I
8 know of no one in the medical or public health community who would earnestly raise any
9 questions about the causal nature of this relationship.

10 **Q. Is this opinion widely held in the public health community?**

11 A. Yes.

12 **Q. Were any other adverse effects discovered by these studies?**

13 A. Yes, the early studies also showed a diminished head circumference for children, a topic I
14 will discuss further in this testimony.

15 **Q. Does this direct association still hold true today?**

16 A. Yes. In fact, cigarette smoking is the single most important factor affecting birth weight
17 in developed countries.

18 **Q. How exactly does prenatal maternal smoking cause a low birth weight in a fetus?**

19 A. While we don't know the exact mechanism of action, we do know that it affects the fetus
20 in several ways. First, as I've described before, it increases the carbon monoxide content both
21 within the mother and child, inhibiting the ability of maternal and child hemoglobin to carry, and
22 ultimately deliver, oxygen to the child. Second, it increases vascular resistance in the placenta,
23 which in itself decreases blood flow to the baby.

24 **Q. How has this resistance been detected?**

1 A. This effect has been detected by fetal ultrasound.

2 **Q. What causes this resistance?**

3 A. This increase in resistance is a result of a decrease in flow through the maternal-fetal
4 vessels. The flow is decreased due to the constriction of the uterine and umbilical arteries (the
5 main source of mother's oxygenated blood for the fetus) by nicotine. By Poiseuille's Law, flow
6 is equal to the change in pressure multiplied by the radius to the fourth power divided by the
7 blood viscosity and vessel length.

$$8 \quad \text{Flow} = (\text{Change in Pressure})(\text{radius})^4 / (\text{viscosity})(\text{vessel length})$$

9 Thus, if the radius is decreased by vascular constriction and all other factors remain constant, the
10 flow through that vessel decreases as well. Resistance is equal to pressure divided by flow
11 ($\text{Resistance} = \text{Pressure}/\text{Flow}$), so therefore if pressure is constant (the pressure of the mother's
12 blood is constant, unless she has an underlying heart or blood disorder) and flow decreases,
13 resistance must increase. This relationship is based off of Ohm's Law, and it is a fundamental
14 tenet of physics and vascular physiology. With decreased blood flow through these vessels, the
15 fetus receives less oxygen from the mother's blood, making it enter into a state of chronic
16 hypoxia, or low oxygen levels for a sustained period of time.

17 **Q. Any other causes for this reduced oxygen delivery?**

18 A. Decreased oxygen delivery to the fetus is also caused by increased levels of hemoglobin
19 bound to carbon monoxide (called carboxyhemoglobin), another effect of nicotine. The more
20 carboxyhemoglobin there is in the fetal circulation, the less oxygen that is delivered to fetal
21 tissues. This state of chronic hypoxia has been documented to cause hypoxic-ischemic
22 encephalopathy, which is a cause of permanent damage to central nervous system cells. In
23 addition to chronic hypoxia's effects on the CNS, it can lead to cardiovascular, hematological,
24 gastrointestinal, pulmonary, adrenal, and metabolic effects.

1 **Q. Any other effects?**

2 A. There are a number of other alterations that have been identified, such as nitric oxide and
3 prostacyclin deficiency, that are associated with maternal smoking and which in itself may affect
4 the uteroplacental blood flow and contribute to impaired fetal nutrition and increased perinatal
5 mortality of babies born to women who smoke.

6 **Q. How does nitric oxide contribute to these conditions?**

7 A. Nitric oxide is a substance that leads to vascular smooth muscle relaxation, thus acting to
8 dilate blood vessels.

9 **Q. What evidence do you have of this?**

10 A. Studies as recent as July 2004 have demonstrated decreased nitric oxide levels and
11 decreased levels of endothelial nitric oxide synthase, the enzyme that synthesizes nitric oxide, in
12 fetal umbilical blood in mothers who smoked during pregnancy. These levels were normal in
13 mothers who did not smoke during pregnancy. In 1991 and 1992, Myatt and colleagues
14 demonstrated that nitric oxide contributes to the resistance level in the fetal-placental circulation.
15 Furthermore, throughout the 1990's, numerous studies have illustrated that nitric oxide and its
16 synthesizing enzyme endothelial nitric oxide synthetase, are decreased in women with
17 intrauterine growth retardation. In 1999, Obwegeser and colleagues demonstrated that maternal
18 cigarette smoking during pregnancy reduced nitric oxide in the fetal blood vessels. In 2000,
19 Chalon et al. demonstrated that nicotine infusion leads to impaired endothelium-mediated
20 vascular relaxation *in vivo*.

21 **Q. How do you explain this decrease?**

22 A. This decrease can be explained by the fact that estrogen and L-arginine, which are
23 precursors of nitric oxide and endothelial nitric oxide synthase, are decreased in the maternal and
24 fetal circulation in mothers who smoke. These studies have also noted that these babies born to

1 smoking mothers who had low nitric oxide levels during gestation also suffered from low birth
2 weight and intrauterine growth retardation.

3 **Q. Why is this important?**

4 A. If nitric oxide is not present in sufficient levels to dilate the fetal blood vessels, the
5 vessels' formation may be impaired and they remain in a state of constriction. This constriction
6 limits the amount of blood, and thus the amount of oxygen and essential nutrients, that the fetus
7 receives. The effects of this were discussed in the last question.

8 **Q. You also mentioned a deficiency in prostacyclin. What is this deficiency's impact on**
9 **fetal growth?**

10 A. Prostacyclin deficiency, like nitric oxide, also contributes to constricting the fetal vessels.
11 Prostacyclin is an inhibitor of platelet aggregation. If there is not sufficient prostacyclin present
12 in the maternal-fetal circulation, platelets can aggregate, or clump, thus making the diameter of
13 the vessels smaller and decreasing flow and causing harm to the fetus. Chronic maternal
14 smoking is also associated with alterations of protein metabolism and enzyme activity in fetal
15 cord blood.

16 **Q. What do you rely on to support this conclusion?**

17 A. A study in 2001 found significantly lower concentrations of several amino acids,
18 including aspartic acid, hydroxyproline, threonine, alanine, alpha-aminobutyric acid, methionine,
19 tyrosine, phenylalanine, and lysine, in fetal umbilical venous blood of smoking mothers
20 compared to nonsmokers. In addition, fetal umbilical plasma alkaline phosphatase was
21 decreased.

22 **Q. How do these deficiencies adversely affect fetal growth?**

23 A. These nutritional and biochemical deficiencies may contribute to fetal growth restriction
24 through fetal malnutrition. The chronic hypoxia discussed above may cause suppression of bone

1 matrix synthesis or placental synthesis.

2 **Q. How is this shown?**

3 A. This is reflected by low osteocalcin and bone alkaline phosphatase, which are enzymes
4 involved in bone formation and bone metabolism, further contributing to decreased fetal growth
5 when compared with nonsmoking mothers.

6 **Q. Are there any other primary effects?**

7 A. Yes, there are. The effects I just discussed may be secondary to irreversible changes in
8 the cellular functions of the trophoblast which in itself may contribute to fetal growth restriction.

9 **Q. What is a trophoblast?**

10 A. The trophoblast is the outer cell layer of the blastocyst. The blastocyst is the term for the
11 human embryo at 6-9 days after conception, when the mass of dividing cells of the embryo form
12 into a fluid-filled cavity surrounded by cell layers. The trophoblast eventually becomes the
13 placenta and the membranes surrounded the fetus. This layer forms into villi, which are finger-
14 like projections that facilitate the exchange of maternal and fetal blood.

15 **Q. You also mentioned a condition called hypoxia. What is hypoxia?**

16 A. Hypoxia refers to diminished availability of oxygen for utilization by the cells of the
17 body. When a mother smokes during pregnancy, there is decreased blood flow to the uterus, as
18 I've described, resulting in less oxygen being delivered to the baby. As I have already described
19 in this testimony, this reduction in oxygen delivery is compounded as I've already described by
20 the binding of hemoglobin in mothers' red blood cells with carbon monoxide, decreasing its
21 availability to transport oxygen to the baby and for the baby's blood to deliver or transport the
22 oxygen to the cellular level.

23 **Q. What happens to the oxygen flow from the uterus to the placenta when a mother**
24 **smokes during pregnancy?**

1 A. The evidence of hypoxia comes from animal studies and human studies showing
2 decreased oxygen being delivered to the placenta as well as from the fact that newborn babies
3 whose mothers smoked during pregnancy are born on average with higher hematocrits.

4 **Q. What evidence is there to demonstrate that this hypoxia occurs?**

5 A. Elevated hematocrit levels show this very clearly. Hematocrit quite simply is the percent
6 of whole blood that is made of cellular material.

7 **Q. Are these effects of maternal smoking paralleled by any other birth situations?**

8 A. Yes. Similarities have been noted between the birth characteristics of smoking mothers
9 and births that occur at high altitudes.

10 **Q. What are these similarities?**

11 A. Basically, small for gestational age babies and increased rates of low birth weight. At
12 high altitudes and in the fetuses of mothers who smoke, the oxygen saturation decreases.
13 Increased incidence of fetal growth restriction may reflect the limits of placenta and fetus to
14 extract oxygen because of the altitude's effects on oxygen levels. A compromised placental-fetal
15 circulation could be unmasked at high altitude because of the effects of the low oxygen levels at
16 these altitudes. As explained earlier, having a decreased amount of oxygen to deliver to the fetal
17 tissues can lead to fetal growth restriction. Thus, the same chronic hypoxia occurs in fetuses of
18 mothers who smoke and mothers pregnant at high altitudes.

19 **Q. When did the scientific community acquire all of this knowledge?**

20 A. There was a scientific paper published in 1966 that discussed active smoking and
21 hypoxia. Also, the Surgeon General's Report cites a study from 1979, published by Davies and
22 colleagues, that noted that abstaining from smoking for 48 hours during the third trimester
23 increased available oxygen to the fetus by 8%. So, this knowledge has existed for some time.

24 **Q. Besides actual problems at birth, are there any lasting effects on the subsequent**

1 **growth and development of children whose mothers smoked during pregnancy?**

2 A. Yes, there are. Studies have shown that infants suffering from low birth weight are at an
3 increased risk for emotional and behavioral problems.

4 **Q. What are some of these problems?**

5 A. The problems include lowered cognitive abilities, hyperactivity, and reading and math
6 disabilities. At least one study has also shown an increase in neurological soft signs which
7 means neurological abnormalities that cannot be tied to a particular brain problem but they are
8 noting that there's been some alteration to brain functioning and development.

9 **Q. Any other consequences beyond low birth weight and emotional/behavioral**
10 **problems?**

11 A. Small head circumference is another significant consequence. Your head circumference
12 at birth and the impact throughout childhood is determined by genetics and brain development.

13 **Q. Why is a small head circumference significant?**

14 A. Without brain development you get smaller heads so when you see a population with
15 smaller heads than another, you have to worry that there has been some damage to brain growth.

16 **Q. What is the evidence?**

17 A. There is animal model data showing that nicotine shifts brain cells from dividing, that is
18 proliferation, and shifts them into the mode of differentiating, that is becoming different types of
19 cells earlier than otherwise would be the case.

20 **Q. Any other evidence?**

21 A. A study by Matte and his colleagues, published in 2001, explored the relationship
22 between birth weight and measured intelligence at age 7. Their study examined 3,484 children in
23 the Collaborative Perinatal Project, a cohort study established to study the relationship between
24 prenatal factors, labor and delivery, and child development through age 7.

1 **Q. How was intelligence measured?**

2 A. The children's intelligence was measured by the Wechsler intelligence scale for children.

3 **Q. What did the study find?**

4 A. The study found that mean IQ increased with birth weight in both sexes across the full
5 range of birth weights (very low birth weight through normal birth weight). This relationship
6 was not due to confounding by any maternal or socioeconomic factors.

7 **Q. Does the small head circumference endure for the children born to smoking**
8 **mothers?**

9 A. Yes.

10 **Q. For how long does this small head circumference last?**

11 A. Research indicates that the differences in head circumference last until at least age 5 in
12 one study (Elwood et al, 1987), age 2 in another (Karatzaa, 2003) and age 1 in another (Ong et al,
13 2002).

14 **Q. Is this wide range of ages a problem for you?**

15 A. No. Despite great variation in studies, they all agree that it is clear that smoking for the
16 duration of the pregnancy causes a decrease in head circumference for at least one year after
17 birth.

18 **Q. Does stopping smoking help in this case?**

19 A. A 2000 study by Lindley, et al. reported that stopping smoking at the 32nd week
20 eliminated smoking-related differences in birth weight and head circumference, but not deficits
21 in crown-to-heel length.

22 **Q. Dr. Weitzman, how has knowledge concerning the developmental consequences of**
23 **children's prenatal and early passive exposure to tobacco smoke been developed?**

24 A. Over the past few decades, new data concerning these consequences has been developed

1 through a series of observational human subject studies using both cross-sectional and
2 longitudinal designs. In addition, these studies used samples that were diverse in terms of
3 ethnicity, culture and potentially confounding characteristics.

4 **Q. What is a confounding characteristic?**

5 A. Confounding characteristics are characteristics that are associated independently with the
6 outcome that you are concerned about and the exposure of the child.

7 **Q. Can you please provide an example?**

8 A. For example, depressed women are more likely to smoke and that depressed women tend
9 to have children with increased rates of mental health and educational problems. So, maternal
10 depression is sometimes a confounder of smoking or smoking is a confounder of studies of
11 maternal depression's effects on child development.

12 **Q. Are you familiar with the epidemiological term "over controlling?"**

13 A. I am familiar with over controlling.

14 **Q. What is "over controlling?"**

15 A. Over controlling is when you use statistical mechanisms and control for things that are
16 influences on the outcome of interest as well as confounders.

17 **Q. How can overcontrolling affect smoking research?**

18 A. With smoking, we know that nicotine is neurotoxic and a neuroteratogen itself and as a
19 consequence leads to increased rates of behavior problems and intellectual problems. We also
20 know that smoking is the number one cause of low birth weight, accounting for 70% of low birth
21 weight and we know that low birth weight itself, causes many, many problems. So when you
22 control for low birth weight, what you are actually doing is being more conservative and setting
23 the bar even higher because you are removing one of the ways in which tobacco actually
24 influences the child. So you are underestimating rather than overestimating the effect of the

1 tobacco which is both direct and via low birth weight.

2 **Q. Earlier, you mentioned a cross-sectional study. What is such a study?**

3 A. A cross-sectional study is one in which you obtain information about the outcome of
4 interest at the same time that you obtain information about the exposure.

5 **Q. Can you please provide an example?**

6 A. With the National Health and Nutrition Examination Survey, you can draw blood from
7 children participating in this study and get measures of cotinine, the major metabolite of nicotine,
8 at the same time you study the child's neurocognition or other outcomes, whether it is the
9 Metabolic Syndrome as I mentioned before, or tooth decay.

10 **Q. What are the limitations of such a study?**

11 A. A single cross-sectional study is limited in its ability to allow you to draw causal
12 inferences because you don't have evidence that the exposure precedes the outcome. You don't
13 necessarily have good evidence about the intensity of exposure over time.

14 **Q. You also mentioned a longitudinal study. What is such a study?**

15 A. A longitudinal study, in contrast to a cross-sectional study, is a study in which
16 information is collected about the exposure before the point of the outcome of interest.

17 **Q. How would such a study work with the issue of maternal smoking and**
18 **neurocognitive deficits?**

19 A. So if you enrolled pregnant women and followed them through the pregnancy and then
20 studied their children longitudinally, you would be able to demonstrate that tobacco exposure
21 occurred before the outcome of interest. That's the major advantage of a longitudinal study over
22 a cross-sectional study. It obviously is much more expensive and takes logistically much more
23 effort.

24 **Q. Which type of study is used more by researchers?**

1 A. Because of the difficulties and the amount of money that is required, researchers use
2 cross-sectional data more often than they do longitudinal data.

3 **Q. In the end, what do these studies generally demonstrate?**

4 A. The cross-sectional and longitudinal studies demonstrate the same sorts of findings:
5 exposure to tobacco smoke leads to increased rates of behavior problems at all ages, increased
6 rates of neurocognitive deficits and decrements in school performance.

7 **Q. With regard to the issue of the behavior of children with smoking mothers, what**
8 **have the studies performed over the years demonstrated?**

9 A. As regards behavior, the studies have shown babies that are more negative, irritable, and
10 fussy. These babies also cry more in the first year of life. In addition, they become toddlers who
11 are more difficult to discipline and more oppositionally defiant during the pre-school years, and
12 demonstrate increased rates of behavior problems of a wide range as well as increased rates of
13 ADHD during the school years. In these subjects' adolescence, there are increased rates of
14 conduct disorders and oppositional/anti-social types of behaviors.

15 **Q. Did these studies account for any potential confounders?**

16 A. Each of these studies attempted to control for potential confounders through use of a
17 multivariate statistical analysis.

18 **Q. What is a multivariate statistical analysis?**

19 A. A multivariate statistical analysis is a series of statistical procedures by which you are
20 able to separate out the independent association of one thing from another when you have
21 something that is as complicated as behavior problems, school performance or educational
22 achievement.

23 **Q. How does it help to control for potential confounders?**

24 A. Control for potential confounders enables one to use epidemiologic mechanisms to

1 identify those characteristics that are independently associated with the outcome of interest. As
2 I've said many times, research is a word in the English language that means exactly what it says –
3 you search and you search again. So no one study, whether it is an animal study or it is a cross-
4 sectional or a longitudinal study convinces everybody that all potential confounders have been
5 controlled for. It is the cumulative evidence used from multiple studies using different
6 mechanisms using different confounders that builds a body of evidence that leads reasonable
7 people to reach reasonable conclusions about the data.

8 **Q. What are these potential confounders?**

9 A. Some of the potential confounders are maternal mental health, maternal IQ, education,
10 poverty level, social supports, affect, low birth weight of the child, lead poisoning, iron
11 deficiency and anemia.

12 **Q. Any specific examples of these studies?**

13 A. Yes. Over the years, there have been at the very least 30 studies exploring cognitive and
14 behavioral functioning in relationship to prenatal tobacco exposure.

15 **Q. What have these studies discovered?**

16 A. In 1981, Nichols and Chen demonstrated a 1.28-times greater risk of increased locomotor
17 and impulsive behavior in children exposed to prenatal tobacco. Two years later in 1983,
18 Rantakallio and colleagues demonstrated a 1.78-times greater risk of delinquency in children
19 whose mothers smoked during pregnancy. In 1991 and 1993, Fergusson and colleagues
20 demonstrated increased conduct disorder, ADHD, and total disruptive behavior in these children
21 after adjusting for confounders. In 1994, McGee and Stanton demonstrated women who smoked
22 during pregnancy reported that their children had high rates of behavioral problems at 5 years of
23 age, even after statistical adjustment for a wide variety of confounding variables. In 1996,
24 Milberger and colleagues demonstrated a 2.7-times greater risk of ADHD in kids exposed to

1 prenatal tobacco compared to those not exposed, and in 1997 Wakschlag and colleagues
2 demonstrated a 3.3-times greater risk of conduct disorder in children of mothers who smoked
3 during pregnancy. In 2003 and 2004, Fried and Watkinson were able to review data from 13- to
4 16-year-old children who had been exposed to tobacco during pregnancy. They showed that IQ
5 was linearly and negatively associated with in utero cigarette exposure, and these exposed
6 children showed decreased attention and increased impulsivity when compared to non-exposed
7 controls.

8 **Q. Any other studies that you wish to discuss?**

9 A. Yes. In the July 2003 edition of the *Journal of Pediatrics*, Robert Kahn and his
10 colleagues published a study examining the effects of a change in the dopamine transporter gene
11 in children and maternal smoking on childhood hyperactivity-impulsivity and inattentiveness.

12 **Q. How did this study work?**

13 A. The study followed 161 children from age 6 months to 5 years using standardized scales
14 of hyperactivity-impulsivity, inattentiveness and oppositional behavior. It determined if the
15 specific change in the gene was present in zero, one or two copies in the children.

16 **Q. What did the study find?**

17 A. It determined that children who had two copies of this gene change and were exposed to
18 prenatal maternal smoking had significantly elevated hyperactive-impulsivity and oppositional
19 scores.

20 **Q. Did you ever personally perform research in this area?**

21 A. Yes. In 1992, a group led by myself noted that after statistical adjustment for
22 confounders, there was an increased rate of behavioral problems among children prenatally
23 exposed to tobacco. Evidence also suggested that there was a dose-response relationship present
24 as well.

1 **Q. What is a dose response relationship?**

2 A. A dose response relationship means that with increased amounts, or doses, of a drug,
3 toxin, or exposure, there is increased presence or severity in the resulting disease process.

4 **Q. Why is such a relationship significant?**

5 A. The relationship is significant because it makes a stronger argument that a particular
6 exposure is involved in leading to a disease if increased rates of the disease are seen with
7 increased amounts of exposure. This occurred in my study, where we determined that the more
8 cigarettes that a mother smoked per day while pregnant, the higher the number of behavioral
9 problems that those children experienced.

10 **Q. In summary, what does the animal model and human epidemiologic data**
11 **demonstrate with regard to the association between prenatal tobacco exposure and adverse**
12 **behavioral and neurocognitive effects on children?**

13 A. The animal and human epidemiologic data are overwhelmingly consistent in
14 demonstrating an association between nicotine, prenatal tobacco and postnatal passive exposure
15 and neurocognitive functioning problems in, and increased rates of behavior and mental health
16 problems.

17 **Q. Isn't it true that differences between smoking and nonsmoking mothers, such as**
18 **increased illicit drug/alcohol use and more depressive symptoms among smoking mothers,**
19 **might explain the adverse outcomes experienced by the smoking mothers' children?**

20 A. No. That is incorrect.

21 **Q. Why is that incorrect?**

22 A. For two reasons. One is that the human epidemiologic studies have controlled for these
23 potential confounders; secondly, the experimental literature with animals which we could never
24 conduct with humans clearly demonstrates that in the absence of illicit drugs, alcohol use, or

1 depression, nicotine or tobacco smoke have adverse outcomes on children.

2 **Q. So, this is a serious child health concern?**

3 A. Yes. This is a very serious problem that warrants further extensive research, public
4 health action, and deliberation. There is, in my estimation, sufficient information to longer wait
5 to protect children from this. The problem is that tobacco is highly addictive and there are forces
6 that act against the medical and public health communities that make it difficult to protect all of
7 our children.

8 **Q. Dr. Weitzman, turning your attention to the subject of secondhand smoke and otitis**
9 **media, will you please first explain the how the ear is built?**

10 A. The part of ear that we can see and that most people think of as “the ear” is the outer ear,
11 including the part you can put a Q-tip into. The middle ear is separated from the outer ear by the
12 tympanic membrane, which is also known as the eardrum. Inside the middle ear, a set of tiny
13 bones called ossicles connect the ear drum to the inner ear where the cochlea transforms sound
14 waves into nerve impulses. The middle ear is open to the outside world via the Eustachian tube,
15 which connects down to the pharynx (the inside of the mouth). So, anything that the nose and
16 mouth get exposed to, the middle ear is exposed to as well.

17 **Q. What does the term "otitis media" mean?**

18 A. Literally, otitis media means inflammation of the middle ear. There are many types of
19 otitis media but the main one we are concerned with is acute otitis media, or AOM, which would
20 usually be referred to as an "ear ache" or "ear infection."

21 **Q. How does otitis media develop?**

22 A. When the middle ear is inflamed for any reason the walls of the Eustachian tube become
23 swollen and thus become narrower and often blocked. When the Eustachian tube is blocked,
24 fluid can collect in the middle ear, and sometimes become infected. In the same way that

1 stagnant water becomes a breeding ground for bugs, whereas flowing water does not, blocked
2 fluid in the middle ear is a good growth medium for bacteria. So, when children are exposed to
3 something that irritates the nose and throat, they are at risk of developing middle ear infections.

4 **Q. What symptoms will generally accompany acute otitis media?**

5 A. Otitis media will be evidenced by ear pain, fever, irritability, and poor hearing.

6 **Q. How would a doctor diagnose acute otitis media?**

7 A. Acute otitis media is evidenced by abnormal findings on examination of the ear,
8 including a red ear drum bulging with entrapped pus. The most common way of detecting this is
9 to use an otoscope, which is a specialized lighted magnifier designed for examining ear drums.

10 **Q. Is otitis media especially prevalent in any one age group?**

11 A. Yes, otitis media is particularly common in young children.

12 **Q. Can you explain why children are particularly susceptible to otitis media?**

13 A. Because of the smaller size of all their anatomical structures, it is easier for the
14 Eustachian tube to get blocked. Also young children may be more susceptible to various
15 infections because of an immature immune system.

16 **Q: Dr. Weitzman, do children get otitis media more frequently than adults do?**

17 A: Yes.

18 **Q: Other than what you have already explained, are there any additional reasons**
19 **children get otitis media more frequently than adults?**

20 A: Yes, the Eustachian tube is shorter and has a more horizontal orientation in young
21 children, so it is less likely to open. Therefore, fluid collects more often within the middle ear
22 space of young children. With age and growth, this tube becomes more vertical, thus allowing
23 for better drainage of the middle ear through the nasal structures. In addition, young children
24 spend more time in a horizontal position, thus influencing proper drainage of the middle ear.

1 **Q. How common is otitis media?**

2 A. Acute otitis media is the most frequently diagnosed ailment, the most common bacterial
3 infection, and the most common single reason for antibiotic therapy in children.

4 **Q. Can you estimate for the Court how many children each year in the United States**
5 **will have otitis media?**

6 A. Each year, there are over 24 million office visits for otitis media in children under 15.

7 **Q. Dr. Weitzman, what are the general ramifications for children and their parents**
8 **upon a diagnosis of otitis media?**

9 A. In general, children who are diagnosed with otitis media will be prescribed antibiotics and
10 will miss some day care or school, meaning that their parents will miss some work. Most of
11 them will get better without any serious consequences. Rarely, however, acute otitis media can
12 lead to mastoiditis and meningitis.

13 **Q. Do the antibiotics used to treat otitis media have side effects associated with them?**

14 A. Yes. Some children will have side effects from the medications and occasionally these
15 will be serious.

16 **Q. What are the side effects of these antibiotics?**

17 A. Many children will get non-allergic rashes with antibiotics; these are generally not
18 dangerous but can be concerning to parents. Allergic reactions to antibiotics, although rare, can
19 be life-threatening. Antibiotics frequently can cause diarrhea, which can then be a separate
20 problem. At a population level, overuse of antibiotics leads to increased prevalence of antibiotic-
21 resistant germs, which then can't be treated if they cause serious infections.

22 **Q. What is "recurrent acute otitis media"?**

23 A. Recurrent acute otitis media refers to the occurrence of three or more episodes of acute
24 otitis media in six months or four episodes in one year.

1 **Q. Is recurrent acute otitis media common in children?**

2 A. Yes, several studies indicate that recurrent acute otitis media occurs during the first
3 several years of life in approximately 20 to 30% of the pediatric population.

4 **Q. How is acute otitis media treated?**

5 A. The standard treatment now in this country is a course of oral antibiotics, like amoxicillin.
6 In the days before antibiotics, the treatment was to poke a hole in the ear drum to drain the pus
7 (tympanocentesis). This technique is still performed by some. Another option is to treat the
8 symptoms with pain relievers like Tylenol or Advil and only use the antibiotics if the infection
9 fails to heal on its own.

10 **Q. Dr. Weitzman, other than acute otitis media, are there any other kinds of otitis**
11 **media?**

12 A. Yes, there is also a condition known as "otitis media with effusion."

13 **Q. What is "otitis media with effusion"?**

14 A. This is sometimes called "serious otitis media," or "glue ear," and is a form of persistent
15 middle ear disease, involving non-purulent fluid behind the ear drum, generally in the absence of
16 fever or ear pain. Children with this condition have a layer of fluid in the middle ear for months
17 on end, like a sink with a very slow drain that always has water in it. This "water in the ear" can
18 act like an ear plug and impair hearing.

19 **Q. How is this type of otitis media treated?**

20 A. It is often treated by an ear-tube insertion (tympanostomy).

21 **Q. Is this a common procedure?**

22 A. Yes. Tympanostomies are the most common surgical procedures carried out on children
23 in industrialized countries.

24 **Q. Could you please describe how the procedure is done?**

1 A. It involves inserting a tiny plastic tube through the ear drum. This tube opens the middle
2 ear up to the outside world via the ear canal and helps to keep the middle ear from getting filled
3 with fluid. One of the ways it does this is by equalizing pressure between the middle ear and the
4 outside world. Otherwise, with a blocked Eustachian tube, a relative vacuum can form in the
5 middle ear and this will tend to suck mucus into the middle ear.

6 **Q. Are there any side-effects caused by this procedure?**

7 A. Generally, the tubes will come out on their own after months or years, but occasionally
8 they get stuck and an additional procedure is needed to remove them. Sometimes a granuloma
9 can develop at the site of insertion and this can lead to bleeding out of the ear canal.

10 **Q. Are there risks associated with this procedure?**

11 A. Yes. It is a surgical procedure requiring anesthesia, and there are always risks associated
12 with anesthesia.

13 **Q. What considerations might a doctor take into account when deciding whether ear
14 tube insertion is warranted for a particular patient?**

15 A. Tube placement can be considered in the management of recurrent acute otitis media,
16 especially when acute otitis media complicates otitis media with effusion and is accompanied by
17 hearing loss or speech delay.

18 **Q. How successful is ear tube insertion in alleviating the occurrence of otitis media?**

19 A. The procedure does not have a 100% success rate, but acute otitis media does tend to
20 occur less frequently in children who have had ear tubes placed.

21 **Q. Dr. Weitzman, turning now from the symptoms and treatment of otitis media to
22 epidemiologic information regarding otitis media, is there epidemiologic data that suggests
23 a connection between secondhand smoke and otitis media?**

24 A. Yes--there is epidemiologic data, which has been reviewed several times by federal

1 agencies, that suggests this connection.

2 **Q. What is the current conclusion regarding the import of this information?**

3 A. The conclusion is that there is a relationship between secondhand smoke exposure in the
4 home and either acute otitis media or otitis media with effusion, particularly among children
5 under 2 years of age.

6 **Q. You mentioned that federal agencies reviewed this information. Which federal**
7 **agencies were you referring to?**

8 A. The Surgeon General reviewed the data in 1986, the National Research Council (NRC)
9 also reviewed it in 1986, the US Environmental Protection Agency reviewed it in 1992, and the
10 National Cancer Institute/California Environmental Protection Agency reviewed it in both 1997
11 and 1999. The different reports all included a review of the data available to date at the times
12 they were written; and they all reached similar conclusions.

13 **Q. How did the agencies review the data?**

14 A. For example, the NCI report reviewed the previous government reports and updated them
15 with additional information. They included in their review the data from the previously
16 published reports as well as added reviews of newer research studies that had been published
17 since the previous reports were written.

18 **Q. What type of additional information was included in the NCI report?**

19 A. The NCI/EPA report was also very thorough, systematically reviewing many different
20 papers and providing a table with information on the scientific strengths and weaknesses of the
21 various individual studies, rather than just a list with a concluding summary.

22 **Q. Have studies about the link between otitis media and second hand smoke been**
23 **published in peer reviewed journals?**

24 A. Yes. In 1998 a systematic quantitative review of 34 papers was published.

1 **Q. What is a systematic review?**

2 A. A systematic review is the application of strategies that limit bias in the assembly, critical
3 appraisal and synthesis of all relevant studies on a specific topic. Systematic reviews focus on
4 peer-reviewed publications about a specific health problem and use rigorous, standardized
5 methods for selecting and assessing articles. A systematic review differs from a meta-analysis in
6 that it does not include a quantitative summary of the results.

7 **Q. Dr. Weitzman, turning your attention to this review, what were the subjects of the**
8 **papers reviewed?**

9 A. The papers reviewed included 11 papers on otitis media, 9 on recurrent acute otitis media,
10 5 on middle ear effusion, and 9 on surgery for otitis media with effusion.

11 **Q. And who are the authors of this systematic review?**

12 A. David P. Strachan and Derek G. Cook from London.

13 **Q. How would you characterize the import of these studies reviewed in this paper?**

14 A. Epidemiologic methods were used to investigate whether secondhand smoke is associated
15 with otitis media, and the overall results of these studies support the hypothesis that secondhand
16 smoke causes otitis media.

17 **Q. How did the authors analyze the studies they reviewed?**

18 A. Quantitative meta-analysis was performed for all the outcomes except for acute otitis
19 media.

20 **Q. What is a meta-analysis in this context?**

21 A. Meta-analysis is a statistical synthesis of the data from comparable studies leading to a
22 quantitative summary of the pooled results.

23 **Q. Why was acute otitis media excluded from the meta-analysis?**

24 A. Acute otitis media was excluded because the studies were too varied in design for

1 meaningful synthesis. Meta-analysis doesn't work if you mix apples and oranges together, so a
2 good deal of judgment is needed in order to apply it properly. Some studies were cohort, others
3 cross-sectional; definitions of exposure and disease varied.

4 **Q. Does this affect your conclusions about acute otitis media?**

5 A. This does not affect my conclusions about otitis media, or the strength of the evidence
6 about its relationship to passive smoking. It just means that one technique for summarizing the
7 evidence was not used for this one outcome in this one paper.

8 **Q. What did Strachan and Cook conclude?**

9 A. The authors concluded that: "[e]vidence for middle ear disease is remarkably consistent,
10 with pooled odds ratios if either parent smoked of 1.48 (1.08-2.04) for recurrent otitis media,
11 1.38 (1.23-1.55) for middle ear effusion, and 1.21 (.95-1.53) for referral for glue ear. Odds for
12 acute otitis media are in the range 1.0 to 1.6. [...] Evidence from different study designs and for
13 different disease outcomes relating to middle ear disease in young children is remarkably
14 consistent in suggesting a modest increase in the risk associated with parental smoking. A
15 pooled odds ratio of the order of 1.2-1.5 reasonably summarizes the effect of either parent
16 smoking on the incidence and recurrence of acute otitis media and the prevalence of middle ear
17 effusion, determined by tympanometry or otoscopy. There is also some evidence that parental
18 smoking adversely affects the long-term prognosis of untreated glue ear."

19 **Q. Dr. Weitzman, I'd like to ask you to explain some of the terms you have used in**
20 **discussing the findings of studies—first, what are pooled odds ratios?**

21 A. The odds ratio is related to the risk of acute otitis media associated with tobacco smoke
22 exposure. An odds ratio of 1 would mean no increased risk. Greater than one means increased
23 risk, less than one means decreased risk. The pooled odds ratio is derived by taking the data
24 from the various studies reviewed and combining them as if they were from one big study. This

1 is useful when one finds multiple studies, none of which is powerful enough by itself to
2 demonstrate statistically significant odds ratios. Combining the data from the small studies
3 together as if they constituted one big study will sometimes allow one to find a statistically
4 significant aggregate odds ratio. This aggregate odds ratio is the pooled odds ratio.

5 **Q. What is selection bias?**

6 A. Selection bias is error due to systematic differences between those who take part in a
7 study and those who do not. For example, one of the studies we reviewed includes only children
8 who never had an ear infection, so this is a group that is not representative of the general
9 population because ear infections are very common. If present, selection bias invalidates
10 conclusions and generalizations that might otherwise be drawn.

11 **Q. What is information bias?**

12 A. Information bias is a flaw in measuring exposure or outcome data that results in
13 differences in the accuracy of information collected between comparison groups. For example, if
14 children exposed to tobacco smoke go to the doctor more often in general for any reason, then
15 they would be more likely to get diagnosed with acute otitis media simply because their ears are
16 seen by doctors more often.

17 **Q. How are the biases you have mentioned best addressed?**

18 A. The best studies reviewed overcame this bias by having standardized follow-up for ear
19 exams in both study groups.

20 **Q. How does this overcome the biases?**

21 A. For example, if you have a cohort study, where you are following children from the time
22 of birth, and some are exposed to tobacco and some aren't, but they all get their ears checked in
23 the same way by the same people at the same ages, and they all have their exposure to smoking
24 measured in the same way, then you won't have information bias. If overall the children in both

groups of the study are generally representative of the population they are part of (with respect to age, sex, medical history, etc.) then you won't have selection bias.

Q. What are confounding factors?

A. Confounding factors, also known as confounding variables, are those factors that are independently associated both with the likelihood of experiencing an exposure, and the outcome of interest. A confounder cannot be an intermediate variable on the causal pathway between the exposure (i.e. tobacco smoke) and the outcome (ear infections).

Q. Did any study you have referred to simultaneously address selection bias, information bias and consider confounding factors?

A. No.

Q. How does that affect the credibility of the results?

A. Even though no single study was perfect, the various studies reviewed complemented one another's shortcomings by addressing different types of bias. Strachan and Cook concluded that where these [biases] have been investigated or excluded in the design or analysis, the associations with parental smoking persist."

Q. Dr. Weitzman, can you please explain this conclusion?

A. It means that even if there is a study where, for example, information bias is a problem, one can't argue based just on that, that all of these studies are invalid. Most of the studies were designed to exclude that particular kind of bias and they still found an association between passive smoking and middle ear disease. So that would suggest that the association in the one study was not just a result of the information bias, because if that were the case, there should be no association in studies without such bias. And the same line of argument goes for the other types of bias.

Q. What were the main recommendations of Strachan and Cook?

1 A. The authors recommended that future studies obtain more objective information about the
2 duration and intensity of exposure to environmental tobacco smoke, including specifically the
3 distinction between prenatal and postnatal exposure. They also recommended objective
4 measurement of exposure with cotinine or other biomarkers. Elsewhere, they have called for
5 experimental studies demonstrating the effect of reducing exposure, although they noted that a
6 useful randomized clinical trial on this topic would require approximately 33,000 children and so
7 it is unlikely that this will ever take place.

8 **Q. Dr. Weitzman, I'm going to ask you to go back and explain parts of your answer to**
9 **the previous question. First, what benefit would objective measurement of exposure**
10 **provide?**

11 A. People tend to lie about embarrassing behaviors when they fill out questionnaires. It is
12 documented specifically that women tend to lie about smoking during pregnancy (i.e. they'll tend
13 to deny being smokers when they actually are). If many of the smokers are labeled in the study
14 as non-smokers, then this will lead to "misclassification bias" and will produce erroneous results.

15 **Q. Dr. Weitzman, what is cotinine?**

16 A. Cotinine is a metabolite of nicotine. That is to say that if your body absorbs any nicotine
17 it needs to eliminate it and one of the byproducts of this chemical breakdown is cotinine, which
18 is then expelled from the system in the urine, but can also be found in the hair or in the blood. So
19 taking hair samples, and measuring the chemical content of cotinine allows one to assess
20 exposure to tobacco.

21 **Q. How is hair cotinine measured?**

22 A. Strands of hair are obtained from the scalp, and then taken to a laboratory where they are
23 washed, dried, weighed, dissolved in chemicals and analyzed by a technique that can quantitate
24 cotinine, radio immunoassay for example. This is not a standard test that can be done in every

1 medical lab.

2 **Q. What are biomarkers?**

3 A. Biomarker is an abbreviation of “biological marker” and is defined as “a cellular or
4 molecular indicator of exposure, health effects or susceptibility.” In this case, cotinine is a
5 molecular indicator of exposure. The use of biomarkers in this way is sometimes called
6 “molecular epidemiology.”

7 **Q. Why are the recommendations of Strachan and Cook of particular importance?**

8 A. First of all, distinction between prenatal and postnatal exposure is important--because in
9 utero damage is likely on the causal pathway between maternal smoking and otitis media, low
10 birth weight is not a potential confounder of the relationship of secondhand smoke with otitis
11 media, but rather is an additional outcome of secondhand smoke, and thus not something to
12 control for.

13 **Q. What is the concern regarding controlling for factors that are likely on the causal
14 pathway between maternal smoking and otitis media?**

15 A. Controlling for factors on the causal pathway will artificially reduce the observed relative
16 risk. This issue is particularly relevant in light of the Stathis study, which did distinguish
17 between prenatal and postnatal exposure, and found that prenatal smoking is more important than
18 postnatal smoking with respect to otitis media risk. Studies that lump together prenatal and
19 postnatal smoking (especially if they “control for” low birth weight and other manifestations of
20 prenatal smoking) are therefore likely to miss a real effect of maternal smoking.

21 **Q. Are there any other reasons that those authors strongly recommended objective
22 analysis?**

23 A. Yes. Objective measurement of exposure with cotinine or other biomarkers is preferable
24 because of the stigma associated with smoking during pregnancy. It is more likely that smokers

1 would be misclassified as non-smokers than the converse, causing a bias in the studies toward
2 finding a smaller risk from smoking. Additionally, many women stop smoking temporarily
3 during pregnancy, however, if that is the critical period for causing the damage that leads to ear
4 problems, then one's current smoking pattern at 1 year or 5 years will not be a good marker for
5 relevant exposure, so studies that only use smoking after birth as a measure of exposure will also
6 find misleading results.

7 **Q. Are there any other ways that these experiments could be handled?**

8 A. Yes. The proper way to study this problem and to help find a solution would be through a
9 trial of exposure reduction. However, the strongest evidence would come from controlled
10 experiments which would be unethical in this case because it would call for exposing children to
11 a poison like tobacco smoke.

12 **Q. Can you describe the materials you reviewed in order to draft the report you**
13 **submitted in this litigation?**

14 A. Yes. For my expert report, I did a new review of literature, searching Medline from 1997
15 to June 2001, using the search terms: tobacco smoke pollution and otitis media. The search
16 terms for text words were: passive, second hand, involuntary, parent, maternal, mother, paternal,
17 father, household, smoke, tobacco, cigarette, tympanostomy, otitis media, middle ear, or glue ear.
18 I also restricted the age range to 0-18 and only reviewed English language articles.

19 **Q. Can you explain what the Medline database is?**

20 A. Medline is an online computerized database indexing almost all the peer-reviewed
21 medical science in the world. It is based on data compiled by the National Library of Medicine.
22 It is continuously updated and can be searched by topic, key word etc. A specific list of topics
23 constitutes the MeSH or medical Subject Headings. For example, the official MeSH for passive
24 smoking or ETS is "tobacco smoke pollution."

1 **Q. Did you review any materials besides those found in the Medline searches?**

2 A. Yes, I also reviewed relevant citations found in the articles within my search, which had
3 not been previously reviewed.

4 **Q. How many articles did your searches produce?**

5 A. My searches turned up 20 articles, however 6 of those I deemed irrelevant for providing
6 evidence about secondhand smoke and otitis media. Hence I focused on the 14 relevant
7 epidemiological studies not included in previous reports.

8 **Q. What did these epidemiological studies demonstrate regarding a link between**
9 **secondhand smoke and otitis media?**

10 A. Three of the 14 studies had a strong design for investigating the secondhand smoke-otitis
11 media association.

12 **Q. In your opinion, Dr. Weitzman, what are the studies that best evaluated the link**
13 **between secondhand smoke and otitis media?**

14 A. The Stathis study from 1999, the Adair-Bischoff study from 1998, and the Ilicali study
15 from 2001 are the studies that best evaluated this link.

16 **Q. What were the "strong designs" you referred to for these studies?**

17 A. The different studies had different elements of strong design and I could discuss those
18 individually. The Stathis study's strong design is in its prospective nature and its high subject
19 number. The investigators enrolled 8,556 at the first prenatal visit and followed them and their
20 children through five years post-delivery to note which children developed middle ear disease
21 and its association with smoking status of the mother during and after pregnancy. Further
22 strengthening this study is its ability to adjust for confounding variables. The Adair-Bischoff
23 study was a case-control design, and identified children as cases for otitis media or controls
24 having very low incidence of otitis media. Parents were interviewed by telephone for various

1 smoking exposures in addition to confounding variables. Further strengthening this study is the
2 fact that 15% of the sample was chosen at random to have hair cotinine measurements, home
3 visits, and physician medical record assessment to strengthen parental interviews. The Ilicali
4 study was also a case-control design, and tobacco exposure was measured using objective urinary
5 cotinine analysis, in addition to questionnaire and physical examination. The use of objective
6 cotinine measurements in the latter two studies strengthens their design.

7 **Q. You have used the term "relative risk." What does this term refer to?**

8 A. Relative risk is often known as "risk ratio," which is the ratio of the risk of disease in the
9 exposed to the risk among the unexposed." The higher the relative risk, the greater the
10 likelihood that the exposure is causally related to the disease.

11 **Q. What were the relative risks found in these three studies you have described?**

12 A. These three studies found relative risks ranging from 1.9 to 3.9. These are higher than
13 those reported in previous reviews.

14 **Q. Can you generally describe the Adair-Bischoff study?**

15 A. The Adair-Bischoff study was a case-control study which was comprised of a population-
16 based probability sample in Canada. The results were determined through logistic regression.

17 **Q. What was the study's focus?**

18 A. The study aimed to determine if there is an association between environmental tobacco
19 smoke and otitis media in pre school aged children.

20 **Q. What is a case-control study?**

21 A. A case control study is "the observational epidemiologic study of persons with the disease
22 of interest and a suitable comparison group of persons without the disease." Controls are those
23 persons who resemble the 'cases' in such respects as age and sex but do not have the disease of
24 interest.

1 **Q. What was the design of the Adair-Bischoff study?**

2 A. The study by Adair-Bischoff employed hair cotinine measurements, home visits, and
3 inspection of physician medical records on a subset of the participants to validate the exposure
4 and outcome information otherwise obtained by telephone interview; they also controlled for a
5 large number of potential confounders in their analysis.

6 **Q. How did Adair-Bischoff study assess exposures to secondhand smoke?**

7 A. To assess exposures, the study involved questioning parents regarding the number of
8 household smokers during the child's first three years of life. The study also noted the number of
9 cigarettes smoked by parents and other household members.

10 **Q. How did the study address outcomes?**

11 A. For outcomes, the researchers asked about ear infections, including recurrent acute otitis
12 media, otitis media with effusion, ear-tube insertion, and use of antibiotics to prevent recurrent
13 acute otitis media. In the end, the study used hair cotinine measurements, home visits, and
14 inspection of physician medical records on a subset of the participants to validate the exposure
15 and outcome information otherwise obtained by telephone interview.

16 **Q. What does the word “confounder” mean in this context?**

17 A. A confounding factor has been defined as a variable that can cause the outcome of
18 interest, is not an intermediate variable, and is associated with the factor under investigation. In
19 this study for example, if crowding and passive smoking are both risk factors for ear infections,
20 crowding may be a confounder, because crowding and smoking tend to go together since both are
21 related to poverty. So if one found an association between passive smoking and otitis, somebody
22 could argue that the smoking is just a marker for crowding and that crowding is the real cause.
23 To take care of this kind of problem, the researchers would control for potential confounders.

24 **Q. Dr. Weitzman, what does it mean for a study to control for confounders?**

1 A. To control for confounders means “to adjust for or to take into account extraneous
2 influences in order to reduce confounding bias.” These statistical adjustments can get
3 complicated but the basic concept is very simple, and comes down to comparing apples to apple
4 and oranges to oranges. If we go back to the example we just mentioned, with smoking and
5 crowding, one would check that one weren’t comparing children in homes with a lot of smoke
6 and a lot of crowding with homes with no smoke and no crowding; one would want the smoking
7 prevalence different but the level of crowding to be the same. If the level of crowding is the
8 same in both groups, but smoking is still associated with more otitis, then the crowding doesn’t
9 explain the differences in otitis associated with smoking.

10 **Q. What were the potential confounders that Adair-Bischoff study controlled for?**

11 A. The study controlled for: age, sex, low birth weight, pre-term birth, history of allergies,
12 history of asthma, upper respiratory tract infection, lower respiratory tract infection, health care
13 use, general health status, family history of respiratory illness, child care, prenatal care, parents’
14 education, income, home ownership, crowding, type of heating, humidity, pets, and chemicals.

15 **Q. Can you summarize the authors’ quantitative findings?**

16 A. Yes. The authors found that “[f]or children living in households with two or more
17 smokers, the odds of middle ear disease were 1.88 (1.12-3.15) compared to controls. Then, they
18 used the number of cigarettes smoked as the exposure measure (10+ vs. fewer) yielded a similar
19 OR of 1.89.

20 **Q. Were these results significant?**

21 A. Yes, these results were statistically significant and indicated that passive smoking
22 approximately doubles the risk of otitis media.

23 **Q. Can you summarize the authors’ conclusions based on those statistical findings?**

24 A. Yes. The authors concluded that environmental tobacco smoke is an important risk factor

1 for middle ear disease in urban pre-school children, even in a relatively affluent population.

2 **Q. In your opinion, Dr. Weitzman, was this a well-implemented study?**

3 A. I believe this was a very important study which used good methodology. It is important
4 to obtain objective information measuring exposure. However, most of the studies don't do that
5 because it is so difficult and expensive. These researchers compromised and came up with the
6 alternative solution of using a 15% subset of the study population to validate the questionnaire
7 results using home visits and hair cotinine as an objective biomarker of exposure. They also
8 double-checked the accuracy of reports about outcomes by reviewing the subjects' medical charts
9 and they found good concordance in this validation study between the different types of
10 measures.

11 **Q. Did they control for potential confounders?**

12 A. Yes. They controlled for a large number of potential confounders. In fact, they may have
13 over controlled by including allergy and asthma since environmental tobacco smoke is long-
14 established as a risk factor for allergy and asthma symptoms. Ironically, that would lead to an
15 underestimate of the environmental tobacco smoke effect.

16 **Q. Dr. Weitzman, in your opinion is this study still good science?**

17 A. Yes, since the overcontrolling would lead to an underestimate of the odds ratio, this
18 makes the study's conclusions that much more cautious and believable

19 **Q. How was this study received by the scientific community?**

20 A. It was well-received. It was published by the *Archives of Pediatrics and Adolescent*
21 *Medicine*, which is the official pediatric journal of the American Medical Association. It has not
22 been refuted by subsequent work.

23 **Q. Dr. Weitzman, will you generally describe the Ilicali study?**

24 A. The Ilicali study was a case-control study designed to determine the effects of passive

1 smoking on otitis media with effusion and recurrent acute otitis media.

2 **Q. Specifically, what was the design of the Ilicali study?**

3 A. The Ilicali study, published in 2001, included children aged three to eight years in Turkey.
4 The study employed an objective definition of both exposure and outcome, with environmental
5 tobacco smoke measurement by urine cotinine and otitis media assessment by direct examination
6 by an ear, nose and throat specialist.

7 **Q. Did the study control for potential confounders?**

8 A. Yes, the study controlled for: the number of persons residing in the same household, sex,
9 age of home, type of home, and wood burning stove.

10 **Q. What were the authors' quantitative conclusions?**

11 A. Children with elevated urine cotinine levels were more likely to have otitis media.

12 **Q. What OR did they find?**

13 A. The OR was 2.29 (1,08-4,85) In other words, passive smoking more than doubled the
14 risk of middle ear disease.

15 **Q. Dr. Weitzman, in your opinion, was this a well-implemented study?**

16 A. The study yielded very strong evidence because it used objective
17 measures of exposure and outcome.

18 **Q. Would have you have any criticisms about this study?**

19 A. Yes. One problem is that the children involved in the study were those who had received
20 ventilation tubes because of recalcitrant otitis media with effusion or recurrent acute otitis media.
21 Therefore, one doesn't really know how bad the otitis media is in the control group, except that it
22 is not bad enough to have required such tubes, so the control group likely contains cases of otitis
23 media with effusion and acute otitis media. In addition, they used a relatively high cut-off for
24 urine cotinine to define exposure (25 vs. 10 ng/mg) so the “unexposed “group likely contains

1 many exposed children.

2 **Q. What is the effect of these features?**

3 A. These features would both lead to an underestimate of the environmental tobacco smoke
4 effect.

5 **Q. Dr. Weitzman, in your opinion, is this study still considered good science?**

6 A. Yes, as with the previous study, when one finds biases that are in the direction of
7 reducing the odds that is considered to be conservative or cautious, rather than cavalier or
8 speculative and is a good sign that the authors are not going out of their way to exaggerate an
9 association that isn't really there.

10 **Q. Was the study accepted by the scientific community?**

11 A. Yes, it was published in *Laryngoscope*, which is the journal of the American
12 Laryngological, Rhinological and Otological [i.e. ENT] Society, and it has not been refuted.

13 **Q. Can you describe the Stathis study?**

14 A. The Stathis study was a prospective cohort study which enrolled women and followed
15 them during their pregnancy, at birth, at six months, and five years post-delivery. Logistic
16 regression analysis was then used to analyze the data while controlling for multiple factors. The
17 study found an association between exposure to tobacco smoke in utero and increased risk of
18 middle ear disease in children.

19 **Q. What is a prospective cohort study?**

20 A. A prospective cohort study is one in which a defined population is selected and followed
21 forward for a period of time. From this single population, it is noted which subjects are exposed
22 to the risk factor being studied and which subjects were not exposed. These two groups are then
23 followed forward in time to compare the incidence of the development of the outcome disease in
24 the exposed and non-exposed groups. The main feature of a cohort study is the observation of a

1 large number of people over a long period with comparison of incidence rates in groups that
2 differ in exposure levels (the two groups are the “cohorts”). Cohort studies are generally
3 prospective, i.e. they start before the disease has occurred and then go forward in time. This is
4 different from case-control studies which start with the disease occurrence (cases) and then ask
5 about preceding exposures. The terms “prospective study” and “cohort study” are often used
6 interchangeably. So, according to some people, “prospective cohort” is redundant.

7 **Q. What is the Stathis study’s design?**

8 A. Stathis and the other researchers studied a large number (7357) of children recruited
9 before birth. They then distinguished prenatal from postnatal smoking while controlling for
10 numerous potential confounders.

11 **Q. Did they control for low birth weight?**

12 A. They did not control for low birth weight or pre-term birth as some other studies did, and
13 that is a strength of the study.

14 **Q. Why is it a strength of the study that they did not control for low birth weight or**
15 **pre-term birth?**

16 A. Because in utero damage is likely on the causal pathway between maternal smoking and
17 otitis media, low birth weight is not a potential confounder of the relationship of environmental
18 tobacco smoke with otitis media, but rather is an additional outcome of passive smoking, and
19 thus not something that requires being controlled for. Controlling for factors on the causal
20 pathway will artificially reduce the observed relative risk.

21 **Q. What potential confounders did the Stathis study control for?**

22 A. The study controlled for: child’s age and gender, maternal age, maternal education and
23 socioeconomic status, breastfeeding history, maternal employment status, marital status, history
24 of day care use, and number of siblings children in the household.

1 **Q. Can you please explain what a logistic regression analysis is?**

2 A. Regression analysis involves finding the best mathematical model to predict y from the
3 x's (where y is the disease outcome and the x's are all the potential risk factors). In
4 epidemiology, the logistic model of regression is commonly used; this is a specific statistics
5 technique.

6 **Q. How does logistic regression analysis provide information for investigators doing**
7 **work like what you have described?**

8 A. This is the mathematical technique that allows one to control for multiple factors at once
9 and obtain an "adjusted odds ratio". So, for example if one just looked at smoking and otitis
10 without looking at any other potential confounders, and found an odds ratio of 2; that would be
11 an unadjusted odds ratio. If after all the risk factors are adjusted for, the odds ratio is still 2, then
12 this is much more meaningful than just looking at the unadjusted number. It allows us to say that
13 after controlling for age, sex, and maternal education etc. there is an independent association of
14 passive smoking and otitis.

15 **Q. Are there particular concerns with respect to the distinction between pre and post-**
16 **natal exposure?**

17 A. Yes. This issue is particularly relevant in light of the findings of the Stathis study, which
18 did distinguish between prenatal and postnatal exposure, and found that prenatal smoking is more
19 important than postnatal smoking with respect to otitis media risk. Therefore, studies that lump
20 together prenatal and postnatal smoking (especially if they "control for " low birth weight and
21 other manifestations of prenatal smoking) are likely to miss a real effect of maternal smoking.

22 **Q. Are there additional reasons why pre and post natal exposure should be**
23 **distinguished?**

24 A. Yes. Many women stop smoking temporarily during pregnancy, but if that is the critical

1 period for causing the damage that leads to ear problems, then current smoking at 1 year or 5
2 years will not be a good marker for relevant exposure. Therefore, studies that only use smoking
3 after birth as a measure of exposure will generate misleading results.

4 **Q. Can you summarize the quantitative findings of the Stathis study?**

5 A. As exposure to tobacco smoke increased, the risk of acute otitis increased with a dose
6 response effect.

7 **Q. Can you explain this?**

8 A. Yes, those who smoked 1-9 cigarettes/day had an OR of 1.6; those who smoked 10-19
9 cigarettes had an OR of 2.6; those who smoked 20 or more cigarettes had an OR of 3.3.

10 **Q. Dr. Weitzman, in your opinion was this a well-implemented study?**

11 A. Overall this was a good methodology, although it employed non-medical definitions of
12 ear disease. It did employ useful epidemiologic definitions, and the sample size was large. In
13 addition, this study distinguished between prenatal and postnatal smoking which made it better
14 than studies which did not draw that distinction, because that has caused some confusion in the
15 past with respect to measuring relevant exposure. This study suggests that previous studies may
16 be mixing apples and oranges by not distinguishing between prenatal and postnatal smoking
17 essentially washing out an effect of maternal smoking by putting mothers who didn't smoke
18 during pregnancy in together with those who did.

19 **Q. What would you characterize as the importance of these three studies taken**
20 **together?**

21 A. These studies together help fill in the information gaps left by the previously reviewed
22 papers since they do provide objective (cotinine) information about the duration and intensity of
23 exposure, and specifically address the distinction between prenatal vs. postnatal exposure.

24 **Q. Did any of the studies you have relied upon in your report have any weaknesses you**

1 **feel should be addressed?**

2 A. Yes. One study (Lubianco Neto, 1999) had a much weaker design than all the others
3 insofar as it was cross-sectional and excluded all children with any previous acute otitis media.
4 This essentially made it like a point-prevalence study.

5 **Q. What is a point-prevalence study?**

6 A. That is where you measure occurrence of disease at one point in time, rather than over a
7 long period. Instead of asking how many ear infections children had in the last year, for example,
8 they just looked at who happened to be having an ear ache at the time of the study contact.

9 **Q. Why is this a problem?**

10 A. Because it makes it impossible to look at long-term exposures and long-term outcomes.
11 Such a design might make sense if environmental tobacco smoke was hypothesized to cause
12 acute otitis media immediately following intermittent exposure, but environmental tobacco
13 smoke is a chronic exposure that is thought to begin causing problems even before birth.

14 **Q. What did the Lubianco study conclude?**

15 A. This study found a non-significant protective effect of environmental tobacco smoke but
16 any results are hard to interpret.

17 **Q. Can you explain what a "non-significant protective effect of environmental tobacco
18 smoke" means?**

19 A. A protective effect would mean that the risk of acute otitis media was actually lower in
20 those exposed to environmental tobacco smoke. Non-significant means that, statistically, the
21 results were likely due to chance.

22 **Q. Why are these results hard to interpret?**

23 A. Yes, they are hard to interpret.

24 **Q. Why?**

1 A. Because the results were statistically non-significant this study is by definition
2 “inconclusive” with respect to a link between environmental tobacco smoke and acute otitis
3 media so nothing should be inferred from it. This is in distinction to a significant “negative”
4 study which is one that would have found a statistically significant protective effect. It is not
5 clear however what one would make of the results of this study even if they had been significant
6 because the design of the study was so bizarre.

7 **Q. Were there any additional problems with design of studies you have relied on?**

8 A. Yes. The ten remaining studies feature some minor problems with design or reporting,
9 but nevertheless provide meaningful information.

10 **Q. Can you summarize those results for the Court?**

11 A. Yes. 4 of the 10 studies reported a significant positive association of environmental
12 tobacco smoke and otitis media (relative risks from 1.3 to 4.6). As for the others, 3 reported a
13 positive association but did not provide numbers documenting significance, and 3 reported a non-
14 significant positive association.

15 **Q. Do you know what it means to pool results from various studies?**

16 A. Yes, as we previously discussed with regards to meta-analysis, it involves counting up the
17 data from the different studies and analyzing them as if they were one big study.

18 **Q. Can you pool the results from those 10 studies?**

19 A. Not meaningfully, because the outcomes, exposure measures, populations, and designs
20 vary so much. In order to do a legitimate meta-analysis, one must start with comparable studies,
21 and not mix apples and oranges.

22 **Q. Are the data, though, consistent with the findings from previous reports?**

23 A. Yes. Indeed, if one focuses on the newest studies with the strongest designs, the risk of
24 acute otitis media and otitis media with effusion from environmental tobacco smoke appears to

1 be even higher than previously reported.

2 **Q. Have you reviewed any reports that hypothesized biologic mechanisms whereby**
3 **environmental tobacco smoke may increase Eustachian tube dysfunction and thereby**
4 **contribute to otitis media?**

5 A. Yes. The California EPA/NCI report hypothesized four such mechanisms:

6 1) A decreased mucociliary clearance that promoted entry of microbes;

7 2) A hyperplasia of adenoids that reduced Eustachian tube patency;

8 3) A mucosal swelling that reduced Eustachian tube patency; and/or

9 4) An increase in frequency of URIs (colds) that caused factors 1-3.

10 **Q. Can you explain each of the hypothesized biologic mechanisms in more detail?**

11 A. Yes. Let us look again at the diagram of the ear. Tobacco smoke is thought to damage
12 the tiny projections (cilia) which sweep out debris from the respiratory tract as well as the mucus
13 membranes which line the respiratory tract. This damage impairs the ability to protect oneself
14 against germs. In addition, any irritation or infection of the upper respiratory tract could cause
15 inflammation of the adenoid and block the drainage of the Eustachian tube. Finally, swelling of
16 the membranes lining the Eustachian tube itself would also block drainage, thereby increasing the
17 risk of stagnant fluid which can cause infection.

18 **Q. Is there any other evidence that secondhand smoke may contribute to otitis media?**

19 A. There is evidence that secondhand smoke impairs immune system function, increases the
20 risk of low birth weight and birth defects, and promotes the growth of oral bacteria, all of which
21 could contribute to otitis media.

22 **Q. What did you conclude through your analysis of the epidemiological studies and**
23 **related articles regarding otitis media and environmental tobacco smoke?**

24 A. The accumulated information on environmental tobacco smoke and both acute otitis

media and otitis media with effusion is highly consistent with a causal relationship and the most recent data suggest that the risk of otitis media is approximately doubled by environmental tobacco smoke exposure, and that heavy maternal smoking during pregnancy is likely the most damaging exposure. This implies significant pediatric morbidity and resulting medical expenditures for otitis media attributable to environmental tobacco smoke.

Q. Dr. Weitzman, let's move on to your next opinion. As a pediatrician, are you familiar with the medical condition known as SIDS?

A. Yes. SIDS is an acronym for Sudden Infant Death Syndrome.

Q. What is it?

A. SIDS is defined as the "sudden death of an infant under 1 year of age that remains unexplained after a thorough case investigation, including performance of a complete autopsy, examination of the death scene, and review of the clinical history."

Q. Is SIDS a rare occurrence in the United States?

A. No. While it kills fewer than 1 of every 1,000 children born each year, it is the number one cause of death for infants between 1 month and 1 year of age.

Q. How do you know that?

A. Data from the National Center for Health Statistics.

Q. Is SIDS a serious problem in the rest of the world as well?

A. Yes it is. In fact, SIDS was particularly high in some other countries like New Zealand.

Q. Has a biologic mechanism for SIDS ever been discovered?

A. A biologic mechanism for SIDS remains unknown. However, through the use of epidemiological research, a number of causes have been identified. In fact, epidemiology has provided the most important and conclusive contributions to an understanding of the disorder.

Q. What are some of the causes for SIDS?

1 A. One major cause has been the prone (on the belly) sleeping position. Following the
2 success of the Back to Sleep campaign, which has significantly reduced the SIDS rate, passive
3 smoking has emerged as a currently recognized cause. Other characteristics involved relate to
4 the mother's behavior or even the infant himself.

5 **Q. Can they be categorized?**

6 A. Overall, they can be placed into three categories. One category involves those relating to
7 the mother or the pregnancy itself.

8 **Q. And what are these?**

9 A. They include maternal smoking, maternal age under 20, poor prenatal care, social
10 deprivation, low birth weight, prematurity, multiple births and being born small for gestational
11 age.

12 **Q. And what is another category?**

13 A. Infant factors, like the male sex.

14 **Q. What is the last category?**

15 A. The last category involves environmental factors like prone sleeping, the winter season,
16 soft sleeping surfaces, loose bedding, and postnatal tobacco smoke.

17 **Q. Of all these listed, have any stood out as being the most serious?**

18 A. Sleeping in the prone position and maternal smoking.

19 **Q. Why do these two stand out for you?**

20 A. Because they have been associated with the biggest attributable risk fraction and because
21 they are potentially preventable.

22 **Q. Let's deal with sleeping in the prone position first. What has occurred to make this**
23 **so important for SIDS?**

24 A. Many studies have been performed all over the world indicating that prone sleeping was a

1 major risk factor for SIDS.

2 **Q. You mentioned the “Back To Sleep” Program. What is this program?**

3 A. The “Back To Sleep” Program is a public health campaign under the direction of the NIH
4 and other partners that encourages parents to place their infants in a supine position (on their
5 backs) for sleeping. Hence the term “back to sleep.”

6 **Q. What was the result of these public health campaigns?**

7 A. A dramatic decrease in the SIDS occurrence rate.

8 **Q. How dramatic was the decrease?**

9 A. The incidence of SIDS has decreased almost 50% in this country since the American
10 Academy of Pediatrics statement on infant positioning in 1992 and the Back to Sleep campaign
11 which started in 1994.

12 **Q. Why was this change from a prone sleeping position so successful in reducing the**
13 **SIDS occurrence rate?**

14 A. Simply because it was successful. The proof is in the pudding. Epidemiology and public
15 health science is about what works. Back to Sleep is based entirely on epidemiology research,
16 not on any basic science work. The best science on SIDS, i.e. the epidemiology, indicated that
17 prone sleeping was a major cause; so it made sense to try out an intervention based on that
18 research.

19 **Q. So, if pediatricians are unsure as to why these campaigns worked, how can we say**
20 **that the reduction in the number of infants sleeping in the prone position was directly**
21 **related to the reduction in the SIDS rate?**

22 A. In every country where a Back to Sleep style campaign has been done, there has been a
23 huge drop in SIDS after, but never before, the supine sleeping campaign was initiated. In the
24 Netherlands in the 1970s, there was a national campaign to promote prone sleeping and SIDS

1 went up. The best explanation for all these experiences as well as the epidemiologic research
2 findings is that prone sleeping is a causal determinant of SIDS.

3 **Q. What impact did these events have on the importance of maternal smoking with**
4 **regard to SIDS?**

5 A. Because of the rapid decline in the practice of prone positioning of infants, coupled with a
6 much slower decline in smoking among young women, passive smoking is now a major
7 recognized cause of SIDS.

8 **Q. Have any studies been performed to determine if maternal smoking is linked in any**
9 **fashion to SIDS?**

10 A. Yes. Many studies have been performed.

11 **Q. And what have those studies shown?**

12 A. That passive smoking, especially postnatal maternal smoking, causes SIDS.

13 **Q. Has the federal government studied this issue?**

14 A. Yes. In the latest Surgeon General's Report, entitled "The Health Consequences of
15 Smoking," the Government undertook a systematic review of the literature regarding smoking
16 and SIDS. The Report concluded that "[t]he evidence is sufficient to infer a causal relationship
17 between sudden infant death syndrome and maternal smoking during and after pregnancy."

18 **Q. Has anyone else studied the data?**

19 A. The World Health Organization, National Cancer Institute, and the Surgeon General have
20 also studied the data.

21 **Q. Can you provide a summary of their findings?**

22 A. Yes. Overall, these reviews have reached the same conclusion, that secondhand smoke
23 causes SIDS. In fact, the Surgeon General's most recent report on the health effects of smoking,
24 published earlier this year, states that there is now enough data to conclude that this link is causal

1 in nature.

2 **Q. Has this issue been studied by many individual researchers as well?**

3 A. Yes.

4 **Q. Let's discuss a few of those studies. Dr. Weitzman, are you familiar with an article**
5 **titled "*Passive Smoking and Sudden Infant Death Syndrome: Review of the Epidemiological***
6 ***Evidence?*"**

7 A. Yes, I am.

8 **Q. Where did it appear?**

9 A. It appeared in the medical journal *Thorax*.

10 **Q. When was it published?**

11 A. It was published in 1997.

12 **Q. Who were the authors?**

13 A. Professor H. Ross Anderson and Derek G. Cook of the Department of Public Health
14 Sciences for the St. George's Hospital Medical School in London, England.

15 **Q. Is this a good article on the association between secondhand smoke and SIDS?**

16 A. Yes, it is.

17 **Q. Why?**

18 A. The journal *Thorax* published a whole series of articles on the health consequences of
19 passive smoking. The authors of these articles performed thorough systematic reviews of the
20 existing literature.

21 **Q. What was the purpose of this paper?**

22 A. The paper was a systematic quantitative review of the literature on passive smoking and
23 SIDS.

24 **Q. How were these studies selected?**

1 A. These were studies with relevant quantitative information, initially identified by a
2 computerized search of the medical literature.

3 **Q. What studies were selected?**

4 A. 39 studies were reviewed, including 10 cohort studies and 29 case-control studies.

5 **Q. What are cohort studies?**

6 A. The main feature of a cohort study is the observation of large numbers over a long period
7 of time (commonly years) with comparison of incidence rates in groups that differ in exposure
8 levels. So, cohort studies start with a group of exposed and another group of unexposed people
9 and then compare the occurrence of disease in the two groups.

10 **Q. What did the 10 cohort studies involve?**

11 A. The cohort studies selected here were either planned epidemiological studies of
12 pregnancy and the perinatal period or cohorts constructed from national or regional databases that
13 contained information about maternal smoking during pregnancy.

14 **Q. Did these cohort studies have any benefits compared to other studies?**

15 A. Yes, cohort studies often provide stronger evidence than case-control studies, because
16 they are generally prospective, so there is less potential for bias in the reporting of smoking and
17 other harmful behaviors. The data often come from large national databases.

18 **Q. Did these cohort studies have any disadvantages?**

19 A. Yes. They often failed to differentiate between prenatal vs. postnatal passive smoking.
20 Overall, they tended to lack detailed information about the postnatal circumstances of the infants.

21 **Q. What is the effect of this lack of information?**

22 A. The distinction between prenatal vs. postnatal maternal smoking is problematic because
23 most women either smoke or do not smoke; the vast majority of mothers who smoke after
24 pregnancy smoked during pregnancy as well, and vice versa. Studies that lump together prenatal

1 and postnatal smoking (especially if they “control for” low birth weight and other manifestations
2 of prenatal smoking) are therefore likely to miss a real effect of maternal smoking. Moreover,
3 many women stop smoking temporarily during pregnancy, but if that is the critical period for
4 causing the damage that leads to problems, then current smoking at 1 year or 5 years will not be a
5 good marker for relevant exposure, so studies that only use smoking after birth as a measure of
6 exposure will also find misleading results. Essentially, the lack of information on postnatal
7 circumstances of the infants means less ability to control for confounders.

8 **Q. What is a confounding factor?**

9 A. A confounding factor has been defined as a variable that can cause the outcome of
10 interest, is not an intermediate variable, and is associated with the factor under investigation.

11 **Q. Can a confounder cause bias?**

12 A. Yes, bias can occur when adjustment is made for any factor that is caused in part by the
13 exposure and is also correlated with the outcome.

14 **Q. How would you deal with a confounder in the context of the smoking issue?**

15 A. If low birth weight (LBW) and secondhand smoke go together and one thinks that low
16 birth weight is the true cause of SIDS rather than secondhand smoke, it would be important to
17 adjust for low birth weight in a study of secondhand smoke and SIDS because the relation may
18 be confounded by this factor. That is to say, secondhand smoke may just be a “marker” for low
19 birth weight.

20 **Q. Is there a risk in doing this?**

21 A. Yes. If low birth weight is caused by secondhand smoke, then it would be inappropriate
22 to control for it because that would bias the study against finding a secondhand smoke effect. In
23 this scenario, low birth weight isn’t an independent cause of SIDS; it’s another effect of
24 secondhand smoke. Controlling for it in this case would be “over-controlling” and would

1 “mask” a true effect of secondhand smoke.

2 **Q. Did this article review other studies?**

3 A. Yes. The article reviewed 29 case-control studies.

4 **Q. What is a case control study?**

5 A. A case control study has been defined as an observational epidemiologic study of persons
6 with the disease of interest and a suitable control group of persons without the disease. The past
7 history of exposure to a suspected cause is compared between cases and controls.

8 **Q. What are “controls?”**

9 A. Controls have been defined as people who resemble the cases in respects such as age and
10 sex but do not have the disease of interest.

11 **Q. Are case control studies prospective or retrospective in nature?**

12 A. Case-control studies are generally retrospective, i.e. starting with present cases and
13 looking backwards in time for exposures.

14 **Q. Are there particular diseases for which such studies are more useful?**

15 A. Yes. They are more useful for relatively uncommon diseases like SIDS.

16 **Q. How did these case control studies work?**

17 A. If SIDS affects one baby in 10,000, then a cohort study would need to follow 1 million
18 infants to get 100 cases, whereas a case control study would start with just the 100 cases and then
19 find 100 or 200 controls for comparison. This is much more feasible, affordable and conducive
20 to getting detailed information.

21 **Q. What were some of the more recent studies like?**

22 A. Some were both very large and very comprehensive in the variables assessed. And these
23 studies yielded the most useful information about postnatal smoking and SIDS.

24 **Q. In looking at all of these studies as a whole, what were the main categories of**

1 **confounding factors that they examined?**

2 A. Among the main factors that were examined were age, parity, gestational age, birth
3 weight, sex of the infant, sleep position, and bedding.

4 **Q. Did all the studies use the same number and/or types of confounding factors?**

5 A. No. There was variation in the number and types of confounding factors.

6 **Q. On the issue of prenatal smoking, how many studies reported it?**

7 A. All but one of the 39 studies.

8 **Q. Are you familiar with the term “odds ratio?”**

9 A. Yes, I am.

10 **Q. What is it?**

11 A. The odds ratio is the ratio of the odds of exposure in the cases over the odds of exposure
12 in non cases in perspective studies. In other words, it is an estimate of the risk ratio.

13 **Q. Can you please provide an example?**

14 A. If 60% of smokers cough, the probability of coughing is 60% but the odds are 60%/40%
15 = 1.5.

16 **Q. What is considered a strong odds ratio?**

17 A. Some people would say anything over 2 is strong but there is no absolute cut-off. From a
18 statistical standpoint, as long as the 95% confidence interval for the OR does not include 1, then
19 it is a significant OR. From a public health standpoint, what matters is the attributable risk.

20 **Q. Why does the attributable risk matter?**

21 A. Stolley and Lasky stated that “[w]hile a high Risk Ratio or OR is important in
22 establishing that an exposure causes a given disease, a lower Risk Ratio can be important as well.
23 For example, a high Risk Ratio of 20 for smokers and lung cancer, a crucial fact in understanding
24 the causal relationship between smoking and lung cancer. The much lower Risk Ratio of 1.2

1 associated with passive smoking [...] and lung cancer is less dramatic evidence for a causal
2 relationship, but it is still important because passive smoking may affect many more people. A
3 Risk Ratio of 1.2 means that passive smoking increases one's risk of lung cancer by 20 percent.
4 To an individual, a 20-percent increase in low risk – say from a probability of 1.0 in a 1,000 to
5 1.2 in 1,000—may not substantially change the overall level of risk. But in the case of passive
6 smoking, since large segments of the population are exposed to passive smoke, a 20-percent
7 increase in risk can result in a substantial increase in the number of people with cancer whose
8 disease can be attributable to passive smoking. A low risk ratio can produce high ARs –large
9 number of affected people—and thus have important consequences for public health.”

10 **Q. What were the results like for those studies that made adjustments for confounding**
11 **factors?**

12 A. The summary estimate for the adjusted OR was 2.11. In other words, prenatal smoking
13 more than doubled the risk of SIDS.

14 **Q. Was the association between prenatal smoking and SIDS affected by whether a**
15 **cohort or case control study was employed?**

16 A. No.

17 **Q. Was a causal relationship between prenatal smoking and SIDS found?**

18 A. Yes. The association between prenatal smoking and SIDS was found to possess many of
19 the characteristics of a causal relationship.

20 **Q. What characteristics are demonstrated?**

21 A. The following characteristics were demonstrated: Consistency across various study
22 designs, environments and investigations; strength of the association; a degree of specificity in
23 relation to other causes of infant death (for other potential causes, secondhand smoke had a much
24 lower OR. Also, the secondhand smoke –SIDS relationship remains after controlling for

confounders.); a dose-response relationship; a temporal relationship; existence of logical plausibility; and coherence with other research showing harm to the respiratory system from secondhand smoke.

Q. What else did the authors conclude?

A. The authors concluded that “[t]he evidence is suggestive of an effect of ETS independent of any intrauterine effect. [...] the epidemiological evidence points to a causal relationship between SIDS and postnatal exposure to tobacco smoke.”

Q. How was this article received?

A. It was received very well by the public health community.

Q. Are the conclusions presented in this article still valid today?

A. Yes, they are. Their findings have not been refuted by subsequent research.

Q. Let's discuss another of those studies. Dr. Weitzman, are you familiar with an article titled "*Risk Factors for Sudden Infant Death Syndrome Following the Prevention Campaign in New Zealand: A Prospective Study?*"

A. Yes, I am.

Q. Where did it appear?

A. In *Pediatrics*, the official journal of the American Academy of Pediatrics and the main pediatrics journal in the United States.

Q. When was it published?

A. It was published in 1997.

Q. Who were the authors?

A. There were many authors who contributed to this article. The primary author was Dr. Edwin A Mitchell, of the Department of Pediatrics at the University of Auckland in Auckland, New Zealand

1 **Q. Is this a good article on the association between secondhand smoke and SIDS?**

2 A. Yes, it is.

3 **Q. Why?**

4 A. The data on the exposures were collected before the occurrence of the SIDS cases
5 studied. In addition, this is a national study with a large database. Finally, the study heads
6 adjusted for a large number of confounders.

7 **Q. What was the purpose of this paper?**

8 A. The purpose of this paper was to identify the causes for SIDS following a national
9 campaign in New Zealand aimed at preventing SIDS. More specifically, there was a focus on the
10 causes of SIDS remaining after so many had been prevented through the cessation of prone
11 sleeping by infants.

12 **Q. Can you please describe this national campaign for me?**

13 A. New Zealand conducted a national public awareness campaign to reduce prone sleeping.

14 **Q. What were these other causes?**

15 A. Maternal smoking was among them.

16 **Q. How did the study work?**

17 A. For two years, from October 1, 1991 through September 30, 1993, data was collected by
18 community health nurses on all infants born in New Zealand.

19 **Q. What type of data was collected?**

20 A. The data included information on infant care practices and the amount of smoking
21 exposure.

22 **Q. How often was this data collected?**

23 A. It was collected twice. The first collection occurred at the nurses' first contacts with the
24 infants, and the second collection occurred when the infants were two months old.

1 **Q. What other data was collected?**

2 A. Data on many potential confounders including maternal factors, pregnancy factors, and
3 infant variables was collected.

4 **Q. When was this data collected?**

5 A. From around the time of birth until about 2 months of age.

6 **Q. During this study, how many SIDS cases occurred?**

7 A. 127 cases were reported.

8 **Q. What did the results show?**

9 A. The OR for maternal smoking and SIDS was around 5. The population attributable risk
10 for this was 45%. In other words, almost half of SIDS cases could have been prevented if
11 maternal smoking were stopped.

12 **Q. What did this mean for the importance of maternal smoking with regard to SIDS?**

13 A. Maternal smoking is the number one cause for SIDS now that prone sleeping has been
14 successfully decreased.

15 **Q. Did the authors have any final conclusions?**

16 A. They concluded that maternal smoking is common in New Zealand and with the
17 reduction in the prevalence of prone sleeping, is now a major cause of SIDS there.

18 **Q. How was this article received when it was published?**

19 A. Very well. It has been cited dozens of times in the literature and as far as I know has
20 never been challenged with respect to its methods or findings.

21 **Q. Are the conclusions reached by the article still valid today?**

22 A. Yes. The findings are based on solid research. Overall it is *more* relevant to today's
23 situation than the studies conducted before "Back to Sleep," such as the ones reviewed by
24 Anderson and Cook that were discussed earlier in this testimony.

1 **Q. Dr. Weitzman, are you familiar with an article titled "*Case-Control Study Of***
2 ***Current Validity Of Previously Described Risk Factors For SIDS In The Netherlands?*"**

3 A. Yes, I am.

4 **Q. Where did it appear?**

5 A. It appeared in *Archives of Disease in Childhood*, the main pediatrics journal in the United
6 Kingdom.

7 **Q. When was it published?**

8 A. It was published in 1998.

9 **Q. Who were the authors?**

10 A. There were several authors for this paper. The primary author was Dr. M.P. L'Hoir, from
11 the University Hospital Utrecht/Wilhemina Children's Hospital in the Netherlands.

12 **Q. Is this a good article on the association between secondhand smoke and SIDS?**

13 A. Yes, it is.

14 **Q. Why?**

15 A. Although the sample size is not as big as one might like, it is a national sample. In
16 addition, it is an interesting study because it made a special effort to look at some of the
17 outstanding questions to be answered, such as the role of postnatal smoking specifically.

18 **Q. What was the purpose of this paper?**

19 A. To assess whether previously established characteristics associated with SIDS retained
20 their validity in the face of the reduced incidence of SIDS.

21 **Q. Did the study categorize them?**

22 A. Yes, it did. They were grouped as "mutable and immutable" for the purpose of the
23 analysis.

24 **Q. What does "mutable" mean?**

1 A. Mutable factors are factors or circumstances that are able to be changed or altered, thus
2 making them amenable to prevention.

3 **Q. What does “immutable” mean?**

4 A. Immutable factors are factors or circumstances that cannot be changed or altered.

5 **Q. What were the mutable factors?**

6 A. Passive smoking, maternal alcohol consumption, breast feeding, changes in infant care,
7 prone sleeping, and bed sharing.

8 **Q. What were the immutable factors?**

9 A. Maternal age, parity, birth weight, and socioeconomic status.

10 **Q. How many subjects participated in the study?**

11 A. 73 cases and 146 controls participated in the study.

12 **Q. Did the study make any adjustments in its statistics?**

13 A. Yes. They adjusted for multiple variables using stepwise multiple logistic regression
14 statistics.

15 **Q. What did the study discover with regard to smoking and SIDS?**

16 A. It discovered that parental postnatal passive smoking yielded a significant result.

17 **Q. How significant was the result?**

18 A. It revealed an odds ratio of 6, an extremely high number by any standard.

19 **Q. What does an occurrence ration of 6 mean?**

20 A. It means that after adjusting for all other factors, children exposed to parental postnatal
21 passive smoking were six times more likely to die of SIDS compared to those children who did
22 not experience this exposure.

23 **Q. What else did it discover on this issue?**

24 A. It discovered that like other past studies, there was a dose-response effect with smoking.

1 **Q. What is a dose-response effect?**

2 A. As the exposure to cigarettes increased from 0, to 1-9 cigarettes per day, to 10 cigarettes
3 or more, the relative risk of SIDS increased from 1 to 2.82 to 5.97, a significant increase in this
4 figure.

5 **Q. How was this article received when it was published?**

6 A. It was very well received.

7 **Q. Are its conclusions still valid today?**

8 A. Yes. The findings are based on solid research. Overall it is *more* relevant to today's
9 situation than the studies conducted before "Back to Sleep", such as the ones reviewed by
10 Anderson and Cook that we just discussed previously.

11 **Q. Dr. Weitzman, are you familiar with an article titled "*A Prospective Study Of*
12 *Smoking During Pregnancy And SIDS?*"**

13 A. Yes, I am.

14 **Q. Where did it appear?**

15 A. It appeared in *Archives of Disease in Childhood*, the main pediatrics journal in the United
16 Kingdom.

17 **Q. When was it published?**

18 A. It was published in 2000.

19 **Q. Who authored the article?**

20 A. There were several authors. The primary author was Dr. Kristen Wisborg of the Prenatal
21 Epidemiological Research Unit for the Department of Gynecology and Obstetrics at the Aarhus
22 University Hospital in Denmark.

23 **Q. Is this a good article on the association between secondhand smoke and SIDS?**

24 A. Yes, it is.

1 **Q. Why?**

2 A. The strengths of this study were its ability to adjust for a number of potential confounders
3 and the fact that the information about smoking during pregnancy was obtained prospectively.

4 **Q. What was the purpose of this paper?**

5 A. To study the association between maternal smoking during pregnancy and SIDS.

6 **Q. How was it to do that?**

7 A. It would do so through the use of prospectively collected data from a university ward.

8 **Q. What was this prospectively collected data?**

9 A. The data originated from a questionnaire collecting information such as the number of
10 cigarettes smoked.

11 **Q. What was the purpose of collecting this data prospectively, or before birth and/or**
12 **the occurrence of SIDS?**

13 A. Recall bias is reduced by obtaining information before the occurrence of SIDS. Given all
14 the negative publicity in recent years about smoking, women whose babies have just died may be
15 expected to deny being smokers if they feel that would make them responsible for their babies'
16 deaths.

17 **Q. One of the information categories involved smoking. How were the different levels**
18 **of smoking classified in the study?**

19 A. They were classified by the number of cigarettes smoked per day. Three categories were
20 created: 0 cigarettes per day, 1-9 cigarettes per day, and 10+ cigarettes per day.

21 **Q. What did the study discover?**

22 A. It discovered that children of smokers had more than 3 times the risk of SIDS, and that
23 the risk of SIDS increased with the number of cigarettes smoked per day.

24 **Q. Did the study adjust for any confounding factors?**

1 A. Yes. It adjusted for parity, alcohol, caffeine, maternal height and weight, education,
2 occupation, marital status and prenatal care.

3 **Q. Did the adjustment for these confounding factors substantially impact the results?**

4 A. The adjustment for these confounders did not change the results.

5 **Q. Was there any reduction caused by any confounding factor?**

6 A. Yes. The adjustment for maternal age marginally reduced the risk from 3.5 to 3.0.

7 **Q. What did the study conclude?**

8 A. That in a population with 30% pregnant smokers, 30-40% of all SIDS occurrences could
9 be avoided if all women stopped smoking during pregnancy.

10 **Q. Were the results of this study accepted by the public health community?**

11 A. Yes, the results were accepted by the community.

12 **Q. Are the results of this study still valid today?**

13 A. Yes. The findings are based on solid research. In addition, like the previously discussed
14 studies, it is *more* relevant overall to today's situation than the studies conducted before "Back to
15 Sleep", such as the ones reviewed by Anderson and Cook that we just discussed previously.

16 **Q. Dr. Weitzman, I would like to discuss the causes of SIDS. Has the medical**
17 **community been able to establish a biological mechanism by which passive smoking causes**
18 **SIDS?**

19 A. No. there are various hypotheses available to establish biological plausibility for passive
20 smoking causing SIDS but there is no established mechanism.

21 **Q. Why not?**

22 A. Because the basic scientists have not yet discovered a biological mechanism for the
23 proximal cause of SIDS.

24 **Q. Dr. Weitzman, in your opinion, is the lack of a biological mechanism for SIDS**

1 **important to your opinion that secondhand smoke causes SIDS?**

2 A. Not really. It would be helpful if it existed, but it is not essential. For the vast majority of
3 medical conditions that physicians treat and prevent, we do not know the biological mechanism
4 of the cause or causes.

5 **Q. Dr. Weitzman, in your opinion, is the fact that no biological mechanism for SIDS**
6 **has been conclusively determined fatal to your opinion that secondhand smoke causes**
7 **SIDS?**

8 A. No, it is not. First of all, I would like to clarify that the proposition that secondhand
9 smoke causes SIDS is not a matter of my subjective personal opinion. What I describe here is
10 the scientific evidence from many rigorous studies. The overall conclusion to be reached from
11 the weight of the best evidence is that secondhand smoke is a major recognized cause of SIDS.

12 **Q. You hold this opinion even though there is no definite biological mechanism for**
13 **SIDS?**

14 A. Yes. Epidemiology has often been way ahead of the biological sciences in discovering
15 ways to fight disease and save people's lives. If what you want is to solve interesting intellectual
16 puzzles, then you can keep doing laboratory experiments forever because there will always be
17 another layer of questions brought up by each answer. Einstein said "as the circle of light
18 increases, so does the circumference of darkness around it." But if you want to save lives, you
19 look at the best evidence available today, you base a treatment idea on that and you test it and
20 keep testing it to make sure it's helping people – you do epidemiologic evaluation research.

21 **Q. And how does this apply here?**

22 A. If you have good data identifying modifiable causes for SIDS, leading to the death of
23 infants, then you should do something with that and save babies' lives. Doing nothing just
24 because no one knows the biochemical or cellular mechanism would be irresponsibly crazy and

1 inconsistent with medical and public health policy and practice.

2 **Q. Can you think of any other instances where the medical community took action with**
3 **regard to a health problem without fully understanding the mechanism?**

4 A. There have been numerous instances where the health community has acted this way.
5 One example that is immediately relevant to the problem of SIDS itself involves the Back To
6 Sleep campaign, but I would be glad to give numerous other examples.

7 **Q. What is/was the Back To Sleep Campaign?**

8 A. As I said earlier, the Back To Sleep campaign was public awareness campaign at a
9 national level in the U.S. to encourage parents to put babies on their backs to sleep (the supine
10 position) instead of on their bellies (the prone position).

11 **Q. Did researchers know why sleeping in the prone position had become such an**
12 **important risk factor for SIDS?**

13 A. Doctors had been recommending the prone position because of a belief that it would help
14 prevent reflux of food from the stomach to the esophagus. Biologically, this made sense but
15 there was no epidemiologic evidence to support such a recommendation. And it did more harm
16 than good, for as prone sleeping increased, SIDS increased. This was seen dramatically and
17 tragically in the Netherlands.

18 **Q. Did they know why sleeping in the prone position significantly increased the risk of**
19 **SIDS?**

20 A. No, they did not.

21 **Q. So, what did the public health community do in response to the discovery of this**
22 **important new information?**

23 A. In New Zealand which performed epidemiology research on SIDS early on, the public
24 health community responded with national prevention programs in 1991. In 1992, the American

1 Academy of Pediatrics officially recommended supine positioning for when babies slept. In
2 1994, the National Back to Sleep campaign was launched.

3 **Q. And what were the results of the Back To Sleep Campaign?**

4 A. A dramatic decrease in SIDS deaths.

5 **Q. How significant was this reduction?**

6 A. The reduction was about 50%.

7 **Q. Any other instances where the medical community took action with regard to a
8 health problem without fully understanding the health problem?**

9 A. Yes. John Snow and Florence Nightingale were preventing deaths from infectious
10 disease before the Germ theory. The two identified a problem, surveyed subjects and recorded
11 their results. This allowed them to identify key public health improvements that saved countless
12 lives. In addition, the British Navy was preventing deaths from scurvy a century before the
13 discovery of Vitamin C. Finally, the link between smoking and cancer was discovered long
14 before the National Cancer Institute was created. I could go on as there are many examples that
15 have saved millions of lives.

16 **Q. Do you have any final opinions regarding secondhand smoke and SIDS that you
17 would like to make?**

18 A. Yes, I do. The accumulated weight of the best evidence on maternal smoking and SIDS
19 is highly consistent with a causal relationship. Given the overwhelming evidence linking
20 maternal smoking to SIDS, it should be a major national health priority to develop effective
21 strategies to reduce smoking generally and among young women in particular.

22 **Q. Thank you, Dr. Weitzman.**